

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

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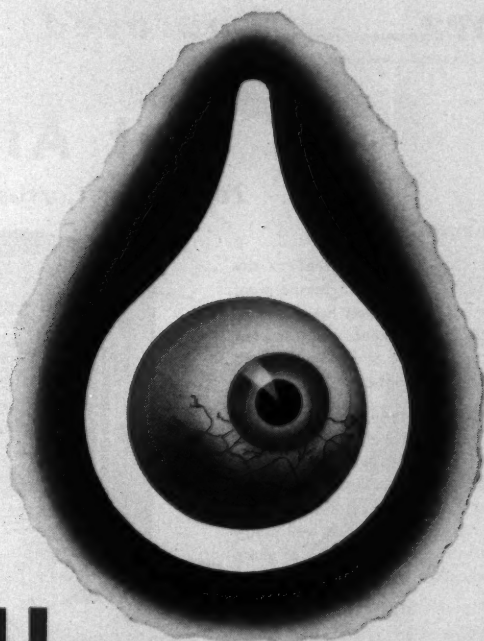
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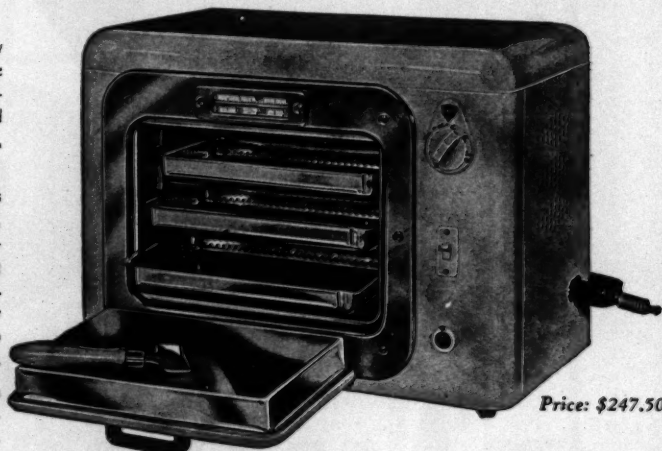
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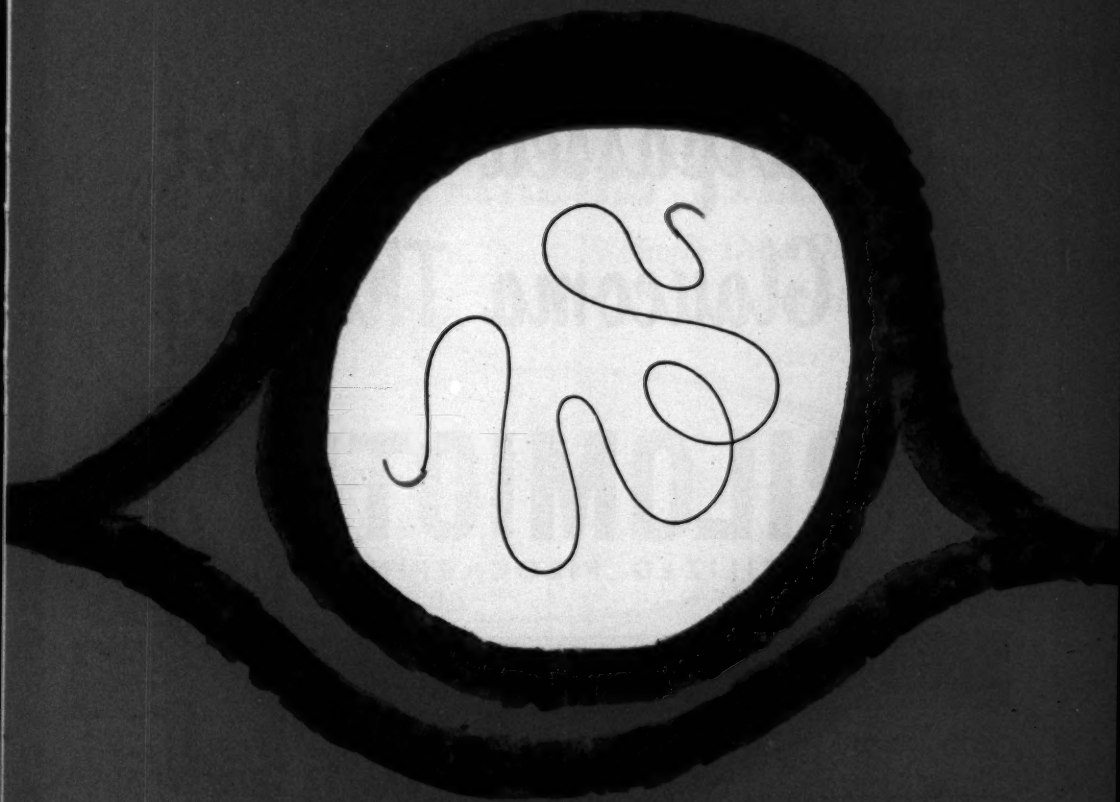
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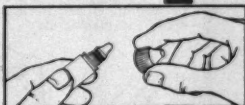
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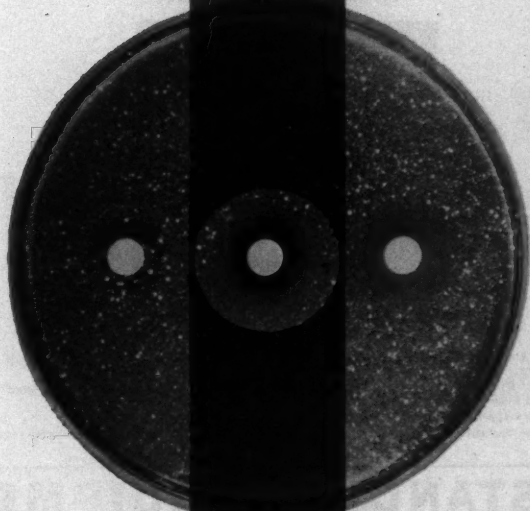
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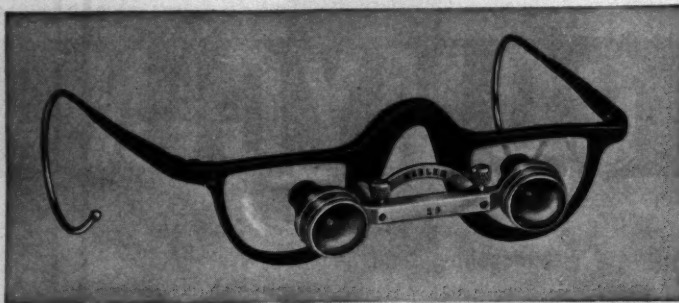
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References: (1) Dickson, R. M.: Brit. J. Phys. Med. 7:77, 1944. (2) Collier, E.: Brit. J. Phys. Med. 6:181, 1943. (3) Mayer, L. L.: A.M.A. Arch. Ophth. 39:232, 1948.

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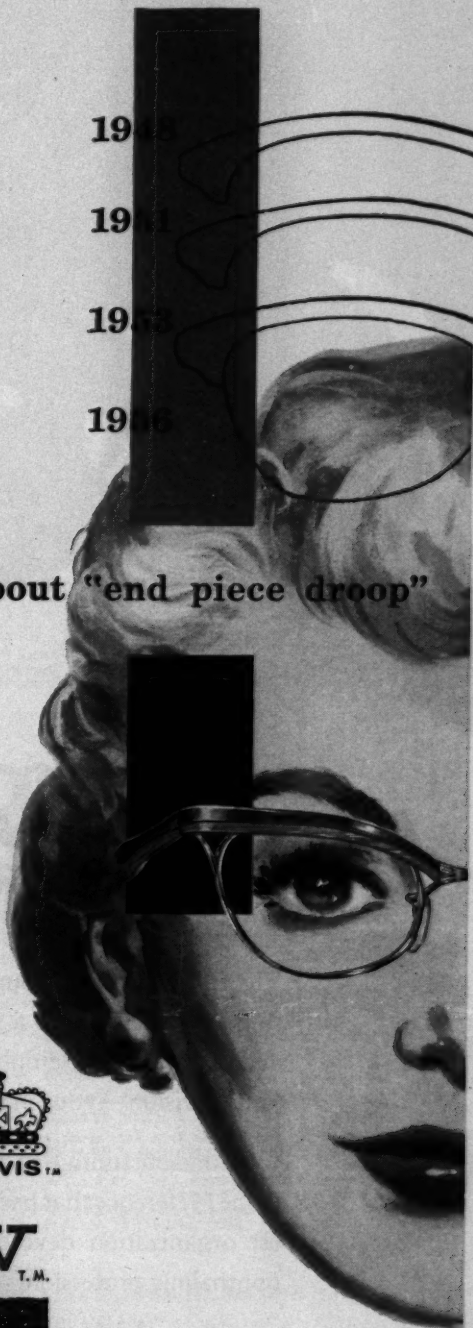


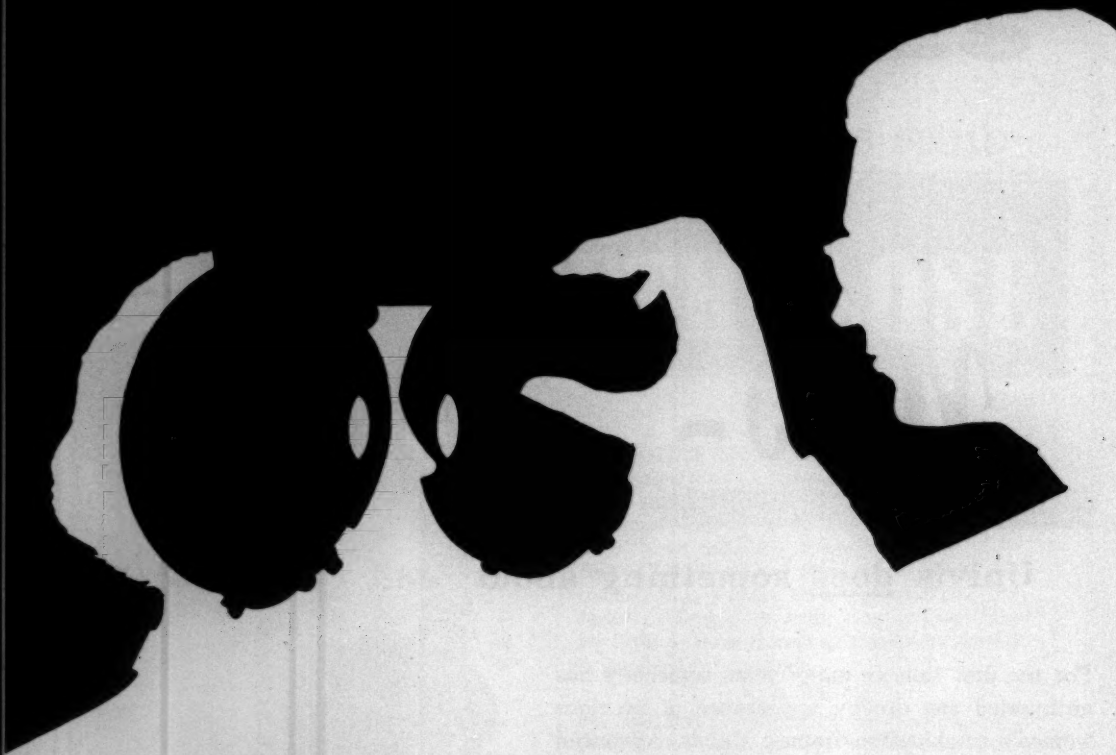
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1. Rasgorshok, R. N. and McIntire, W. C.: *Am. J. Ophth.* 40:34 (July) 1955. • 2. Ehrlich, L. H.: *N. Y. State J. Med.* 53:3015 (Dec. 15) 1953. • 3. Gattas, S. C.: *A.M.A. Arch. Ophth.* 51:467 (April) 1954. • 4. Council on Pharmacy and Chemistry: *J.A.M.A.* 156:1523 (Aug. 27) 1955. • 5. Stelzer, I. H.: *Am. J. Ophth.* 36:116 (Jan.) 1953.

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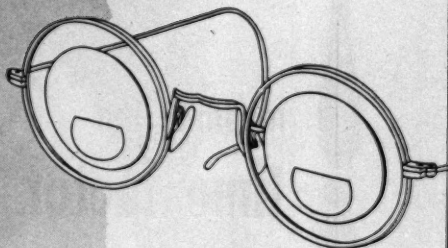
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1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.
4. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1598.

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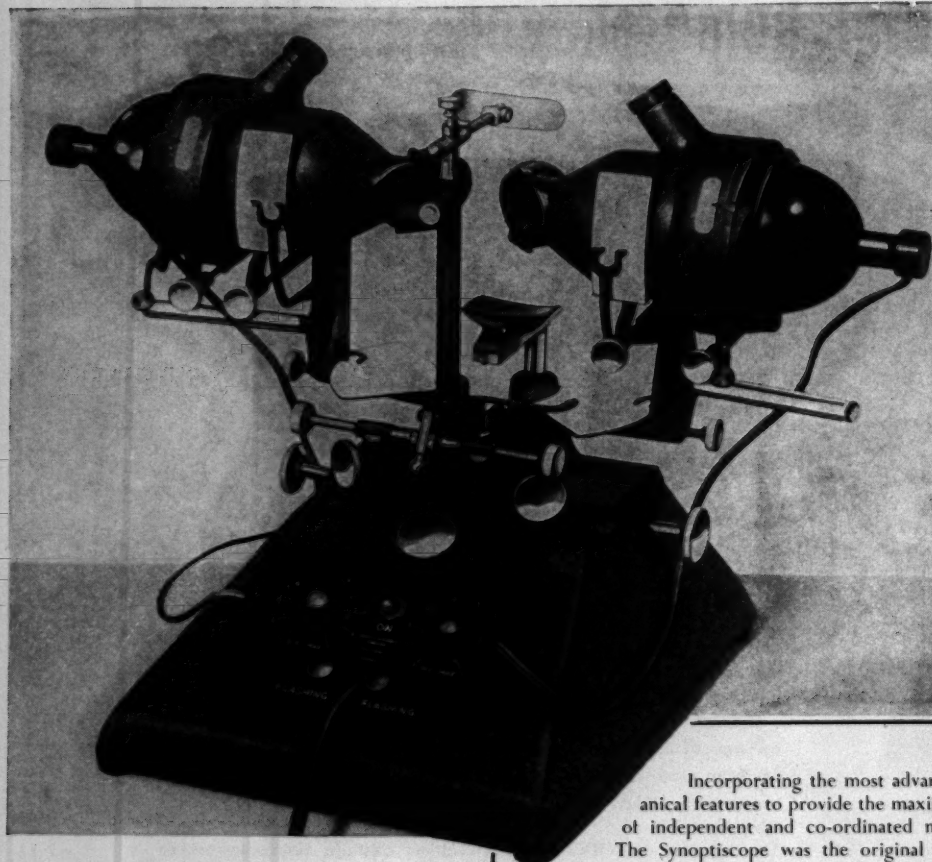
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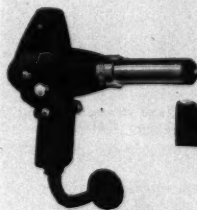
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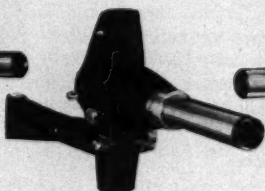


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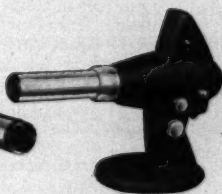
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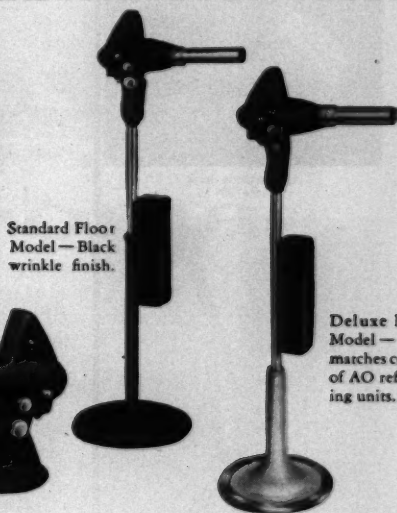
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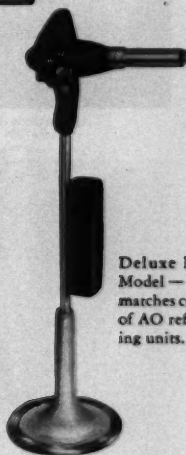
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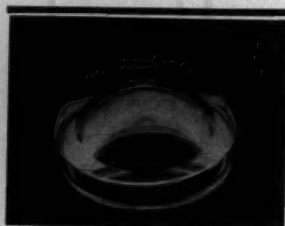
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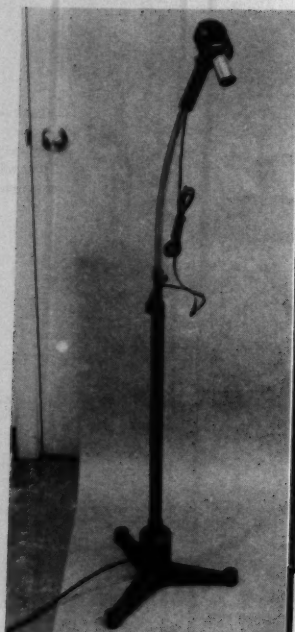
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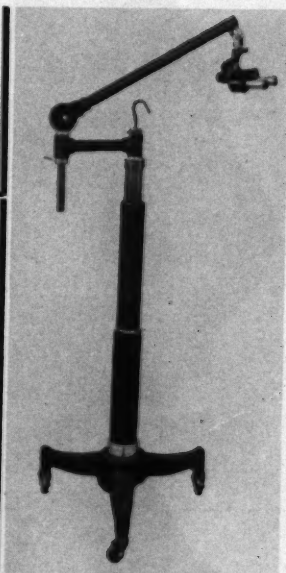
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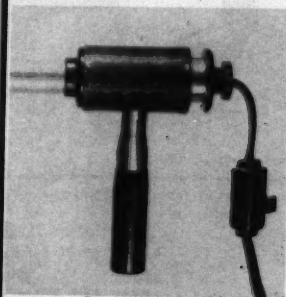
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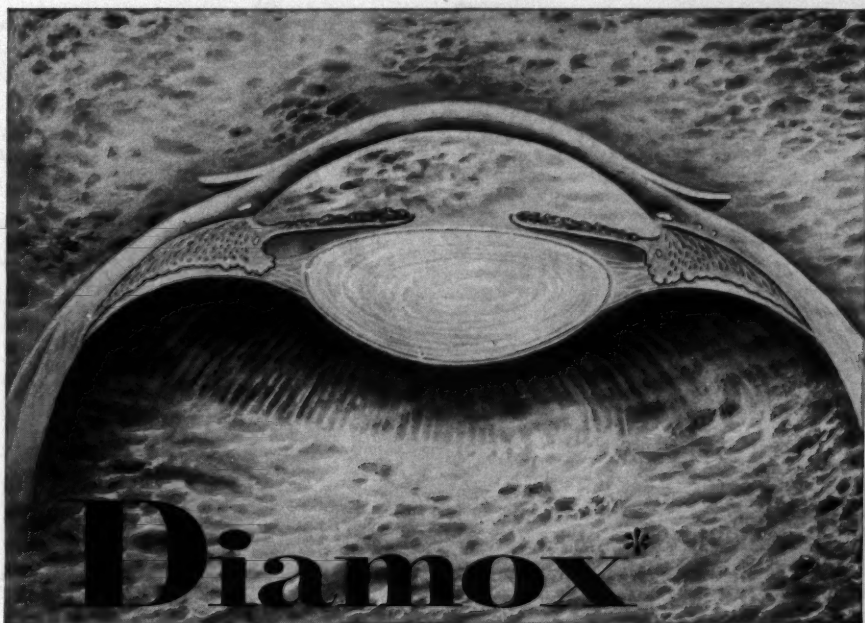
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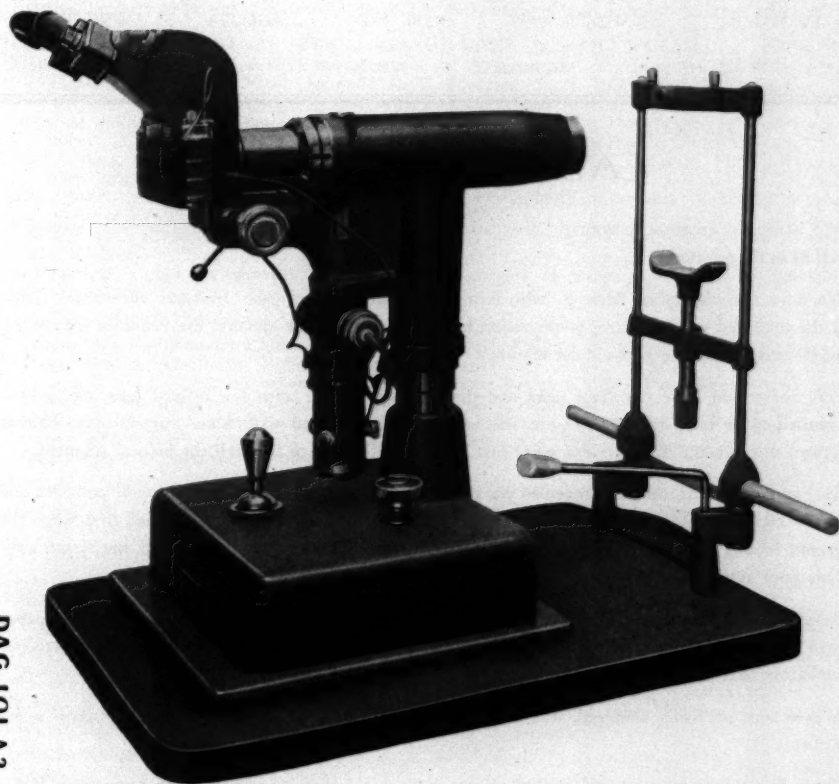
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This correction gave excellent near and distance vision but, with the bifocal lens, the patient complained at once that everything she looked at was tinged with blue. Surprisingly, objects viewed through the distance lens were just as blue as those seen through the bifocal segment.

An examination of the lens revealed no grinding defects. The surfaces were well polished and the correction and axis were perfect. However, a check of the centering revealed that when the patient looked straight ahead the optical center of the lens was 3 millimeters off the visual axis. This poor centering resulted in 6 prism diopters of error.

Before making a new lens for Mrs. S. this prism was neutralized by placing a 6 degree prism base in over the lens to offset the 6 degree error which was base out. The patient reported immediately that the blue cast was gone.

A new lens, perfectly centered, was made and the patient reports no chromatic aberration whatsoever.

Cases like this point up the fact that proper centering is just as important in monocular fitting as in binocular fitting. Too often, badly centered lenses are passed on to the patient with the false justification that since only one eye was being used the centering was of no importance.

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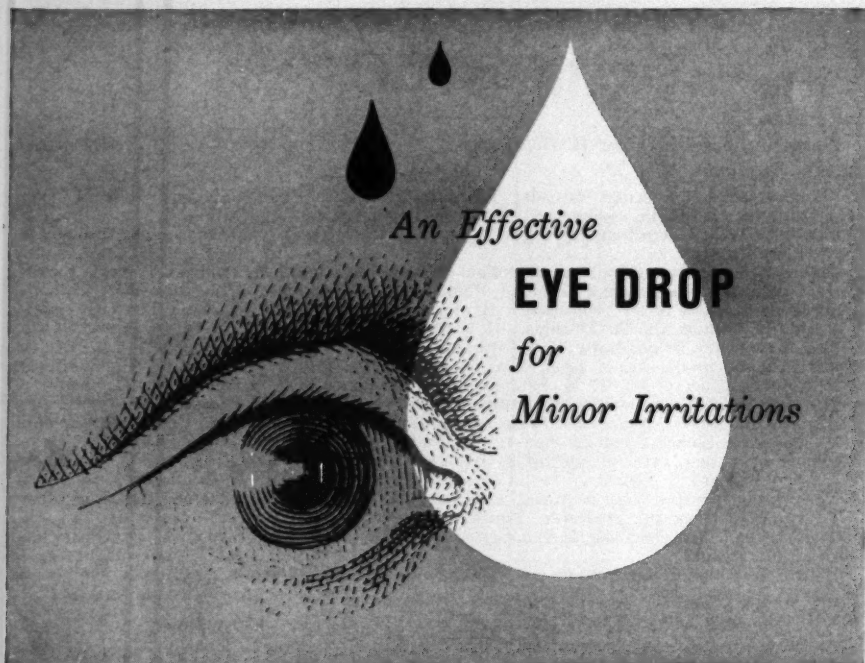
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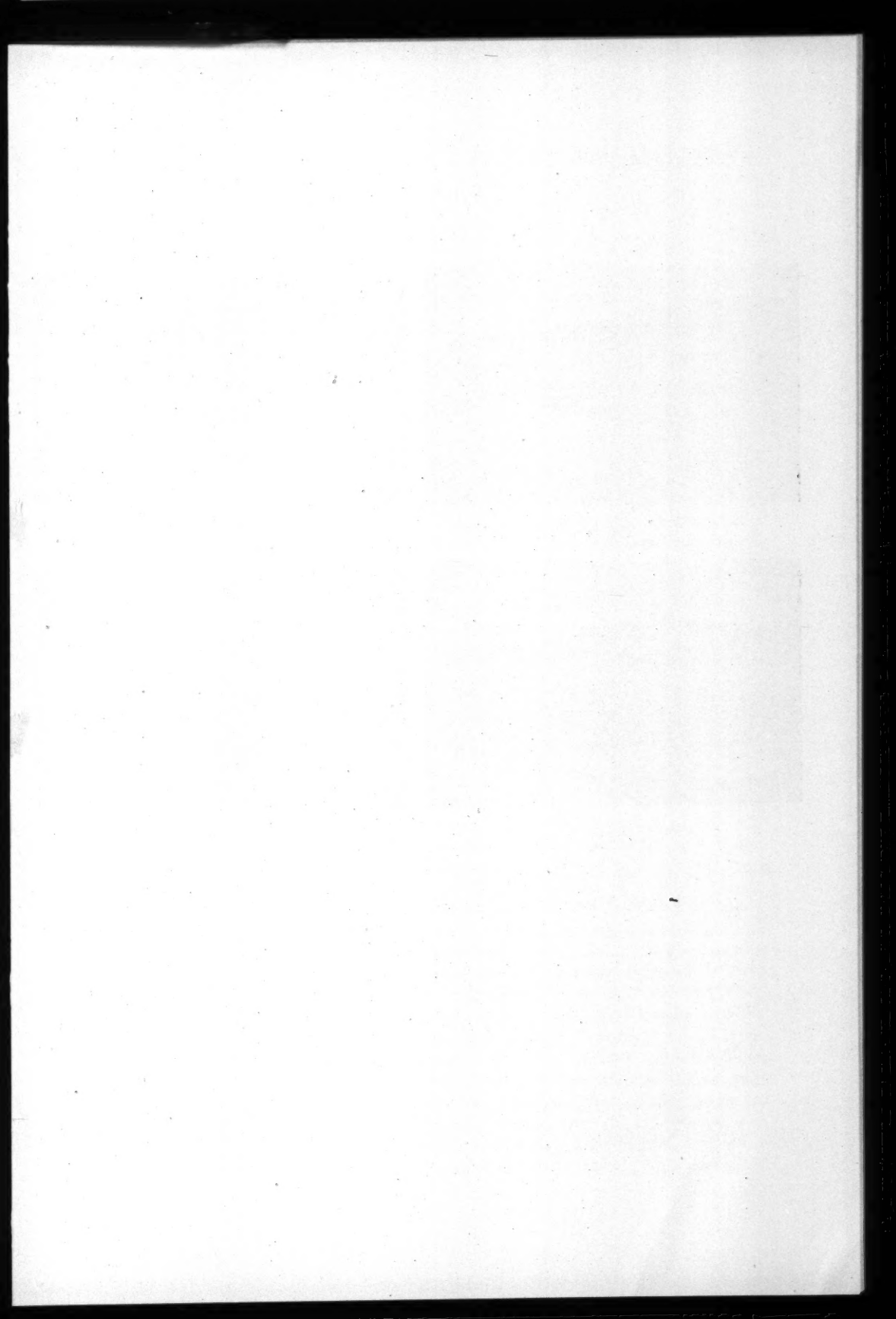
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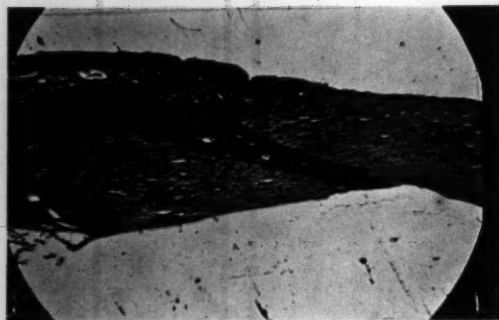


Fig. 1

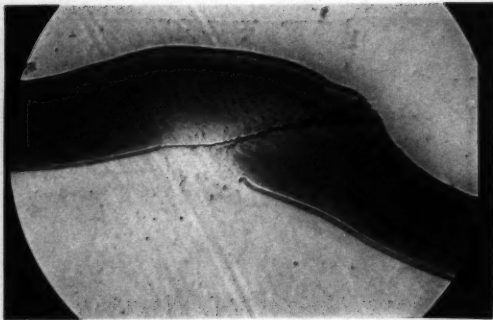


Fig. 2

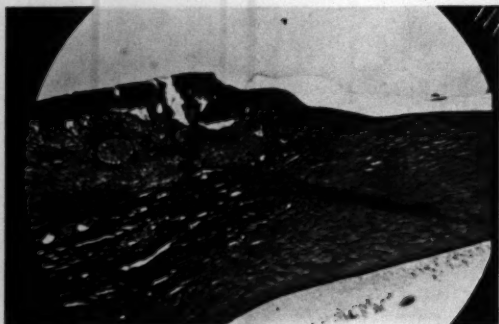


Fig. 3



Fig. 4

Figs. 1-4 (Dunnington). Tissue responses in ocular wounds.

Fig. 1. Eye of a monkey, 10 days after operation, showing a limbal section with a metachromatic substance throughout the entire incision.

Fig. 2. Eye of a cat, 24 hours after operation, showing a corneal section with loss of metachromatic substance along the edges of the incision.

Fig. 3. Eye of a monkey, seven days after operation, showing a limbal section with reticulin fibers throughout the incision.

Fig. 4. Eye of a monkey, 10 days after operation, showing a limbal section with immature collagen fibers throughout the incision.

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TISSUE RESPONSES IN OCULAR WOUNDS*

THE ELEVENTH FRANCIS I. PROCTOR LECTURE

JOHN H. DUNNINGTON, M.D.

New York

(With the assistance of ELLEN F. REGAN, M.D.)

To Dr. Francis I. Proctor all ophthalmology owes a debt of gratitude. This humane physician and his wife devoted much of their time and effort to the study of the ocular diseases of the underprivileged American Indians. Out of their travels came an abiding interest in trachoma and allied diseases and a great desire to see unravelled some of the problems in ophthalmology. The fruition of these aims was the establishment of one of our best research laboratories. Created by their generosity, guided by their ideals, this center of investigation stands as a permanent reminder of Dr. Proctor's great interest in the advancement of ophthalmology. It is therefore both a privilege and a pleasure for me to honor his memory with this lecture.

For centuries surgeons have been intimately concerned with the reaction of tissue to injury. Numerous histopathologic studies have been made on all types of wounds and many factors altering the responses of tissues carefully analyzed. In previous communications we have described the effect of such agents as thrombin and sutures upon the healing of ocular wounds and discussed both normal and abnormal repair.^{1,2} Since these reports, newer investigative methods have revealed significant events

do occur in the early stages of healing. From histochemical studies, chemical analyses, and observations with the electron microscope it has been learned that much activity takes place during the so-called lag phase. This initial period of three days, formerly considered to be a relatively inert one, is now regarded as an important link in the healing process, for it is during this time that the "building blocks" of repair are laid down.³ It is to the nature and importance of these early responses that this presentation will be devoted.

GENERAL CONSIDERATIONS

For a clear understanding of the early happenings in any healing wound it is advisable to review briefly the present day thoughts on connective tissue. It has long been recognized that this tissue consists of cells and a network of fibers imbedded in a homogeneous matrix. Recent investigations have given us more detailed and precise knowledge on the fibers and ground substance of connective tissue. Porter and Vanamee and others have shown that collagen, elastic and reticulin fibers, although differing in their staining and chemical characteristics, have great physical similarities when studied with the electron microscope.⁴⁻⁶ Collagen fibers are coarse, inelastic and insoluble, while elastic ones are thin, elastic, and soluble. The reticulin type, although inelastic, are much smaller than the collagenous ones and possess a special staining affinity for silver preparations. Because of the similarity

*From the Department of Ophthalmology of Columbia University, The Institute of Ophthalmology, Presbyterian Hospital. Presented at the University of California Medical Center at San Francisco, December 7, 1956.

in chemical structure between the reticular and collagenous fibers the former are frequently spoken of as precursors of collagen or procollagenous fibers.^{3,7,8}

The collagen fiber has aroused the greatest interest and its role in disease and in wound healing has been widely studied. Much controversy has centered around its source, but at the present time most evidence supports the theory that it results from an interaction of intra and extracellular substances.⁹ Porter and Vanamee believe that a reaction takes place between fibrils laid down along the cellular membrane and materials found in the ground substance.⁴ Although others, notably Wassermann, have modified this theory, it is generally agreed that the important activating factor in the ground substance is a mucopolysaccharide.⁸⁻¹⁰

Biochemists and histopathologists, alike, emphasize the importance of the ground substance and especially its mucopolysaccharide components. This matrix, once considered an inert amorphous mass, now is known to consist of tissue fluids, mucopolysaccharides, and mucoprotein complexes, and to be metabolically active.^{8,10,11} Gersh, in his many interesting reports, has described the ground substance as an optically homogeneous structure which though normally a gel may become a fluid.¹²⁻¹⁴ Its consistency varies with age, its degree of activity, or the pathologic condition of the tissue. Much of this change is determined by the state of the polysaccharides present in the ground substance. Under certain conditions, such as injury, these mucopolysaccharides may develop metachromasia, a property defined as existing "when a pure dye stains a tissue section in a hue perceptibly different from the color characteristically associated with the dye."¹⁵

Continuous with the ground substance is a so-called cement substance, a protein-carbohydrate complex which binds together the microscopically visible fibrils. Recent investigations have shown that ground and cement substances are essentially one and the same although their chemical components may vary in different parts of the body.^{8,13}

There are two schools of thought about the source of ground substance: Asboe-Hansen and Sylvén believe the mucopolysaccharides of ground substance are products of the mast cells, while others, notably Wislocki, Bunting and Dempsy, and Wassermann, say that they are secretory products of fibroblasts.^{8,16-21} It has been suggested that the so-called mast cells are actually young fibroblasts.³ In any case both ground substance and fibroblasts are intimately connected with the formation of collagen. Dunphy and Udupa have summarized most succinctly the current belief in these words—"The ultimate formation of collagen which provides tensile strength to a wound is dependent upon two factors: a protein component probably produced by fibroblasts, which passes through several stages before becoming collagen; and a carbohydrate component, . . . a complex mucopolysaccharide produced either by mast cells or connective tissue cells."³ Collagen results from the interaction of these two substances.

As a result of recent studies of connective tissue the histologic changes taking place during wound healing have been reinvestigated largely to determine the role played by ground substance and collagen. Both new and old staining techniques have been utilized, notably by Sylvén, Balazs and Holmgren, Wislocki and Bunting, Piriani and his confreres, and Abercrombie and his associates.^{17,18,22-25} Very interesting reports have been published by Dunphy and Udupa.³ They have attempted to measure the sequential formation of mucopolysaccharides and collagen in abdominal wounds of rats. In these experiments they used histochemical methods (toluidine blue, periodic acid-Schiff, and Hale's colloidal iron stain) to demonstrate the presence of mucopolysaccharides, and Van Gieson's and Mallory stains and Neuman and Logan's technique of chemical assay for hydroxyproline for the detection of collagen. Their studies showed that the content of mucopolysaccharides becomes greatly increased during the early stages of repair and reaches its peak about the fifth or sixth

day at which time the first chemical and histologic evidence of collagen fibers appears. As the collagen forms, the hexosamine content of the wound decreases steadily and there is "a remarkably good correlation between the gain in tensile strength and the appearance of collagen." From these observations they concluded that great activity starts in the ground substance within a few hours after injury but no gain in tensile strength occurs prior to the formation of collagen.

SPECIAL CONSIDERATIONS

Inasmuch as most studies on connective tissue have been carried out in nonophthalmic fields it has been necessary to discuss first the findings of the general biochemist and histologist before considering the special problems presented by the ocular tissues. The histologist classifies the substantia propria of the cornea and the sclera as fibrous membranes because in them are found "the typical mammalian connective tissue protein (collagen)," a polysaccharide of the mucin type and elastic and reticulin fibers.²⁶

In the cornea the fibers are small, regularly arranged, and intimately connected with the ground substance. The latter is abundant in supply and contains a large amount of keratosulfate, a mucopolysaccharide found only in the cornea. According to Meyer two other mucopolysaccharides, chondroitin and chondroitin sulfate A, are also present.²⁷ Because of these mucopolysaccharides the corneal stroma is strikingly metachromatic.

On the other hand the scleral fibers vary in size, are irregularly arranged, and can readily be separated from the scant ground substance.^{26, 28, 29} The sclera contains few mucopolysaccharides, no keratosulfate, and normally shows little or no metachromasia. As a transitional structure the limbus shares this lack of metachromasia although its fibers are more regular in their arrangement.

EXPERIMENTS

The studies are an attempt to establish the pattern of normal healing of a limbal

wound. We realize differential staining of connective tissues presents numerous problems both in technique and in interpretation. Nevertheless this method was selected as best suited to demonstrate the significance of the early changes. The experimental animals were the Rhesus monkey (*Macaca mulatta*) and the cat.

A two-mm. limbus-based conjunctival flap was prepared and a cataract incision was made with keratome and scissors. Two appositional postsectional sutures of mildly chromicized surgical gut (6-0) were employed along with a sufficient number of supplementary conjunctival sutures to close the wound adequately.

The animals were killed one, three, four, five, seven, 10, 12, 14, 21, and 28 days after operation. The eyes were removed and were fixed in Zenker's solution. Serial sections were stained with Wilder's silver carbonate and van Gieson methods.

In another study corneal or limbal incisions were made with a keratome or Graefe knife, the animals were killed eight, 24, 48, and 72 hours after operation, the eyes were removed and fixed in four-percent lead acetate and seven- to eight-percent formalin solution. They were sectioned serially and were stained with toluidine blue to determine the time at which the first changes in the metachromasia appeared.

The following staining techniques were used:

A. TOLUIDINE BLUE STAIN^{17, 30, 31}

Solutions

I. Fixing solution.

Mix equal volumes of eight-percent basic lead acetate solution and 15-percent formalin solution.

Fix material 12 to 24 hours. Wash 24 hours in running tap water.

II. Staining solution.

0.1-percent toluidine blue in 1.0-percent alcohol. Adjust to pH 3.7.

III. Mordant solution.

1.0 cc. formaldehyde in 100 cc. of 80-percent alcohol.

Staining Method (paraffin sections)

1. Place sections in two changes of toluene, five minutes each.

2. Place sections in toluene-absolute alcohol solution (equal volumes of each). While in this solution clean slides on both sides.
 3. Pass sections through three changes of absolute alcohol, one to two minutes each. Stand slides to drain.
 4. Dip sections in 0.3-percent cellulose. Stand slides to drain.
 5. Place sections in 95-percent alcohol for two to three minutes.
 6. Mordant sections for 30 minutes in formaldehyde-alcohol solution.
 7. Stain in toluidine blue solution for 30 minutes (in refrigerator).
 8. Wash in three changes of 95-percent alcohol until no color comes from sections.
 9. Mount in 95-percent alcohol. Dry slide and ring coverslip with vaseline.
 10. Let sections dry and mount with permount.
- B. WILDER'S SILVER IMPREGNATION METHOD²³**
- Solutions*
- I. Staining solution
Ammoniacal silver hydroxide solution. To 5.0 cc. of 10.2-percent aqueous solution of silver nitrate add 26 to 28-percent ammonia water drop by drop until the precipitate which forms is dissolved. Add 5.0 cc. of 3.1-percent sodium hydroxide and just dissolve the resulting precipitate with a few drops of ammonia water. Make the solution up to 50 cc. with distilled water.
 - II. Reducing solution
50 cc. distilled water.
0.5 cc. formalin, neutralized with magnesium carbonate.
1.5 cc. uranium nitrate, 1.0-percent aqueous solution.
- Staining Method*
1. Place sections from water into 0.25-percent aqueous solution of potassium permanganate or in 10-percent aqueous solution of phosphomolybdic acid for one minute.
 2. Rinse in distilled water.
 3. Place in hydrobromic acid (Merck's concentrated, 34-percent, one part; distilled water, three parts) for one minute. Hydrobromic acid may be omitted if phosphomolybdic acid is used in Step 1.
 4. Wash in tap water, then distilled water.
 5. Dip in a 0.1-percent aqueous solution of uranium nitrate (sodium-free) for five seconds or less.
 6. Wash in distilled water 10 to 20 seconds.
 7. Place in the ammoniacal solution for one minute.
 8. Dip quickly in 95-percent alcohol—three changes.
 9. Reduce for one minute in the reducing solution.
 10. Wash in distilled water.
 11. Tone in 1:500 aqueous gold chloride (Merck's reagent) for one minute.
 12. Rinse in distilled water.
 13. Place in 5.0-percent aqueous solution of sodium thiosulfate three to five minutes.
 14. Wash in tap water.
 15. Counterstain, if desired, with alum hematoxylin and van Gieson's stain or alum hematoxylin and phloxine.
 16. Differentiate and dehydrate in 95-percent followed by absolute alcohol.
 17. Clear in xylol and mount in balsam.
- Celloidin sections are cleared in oil of originum following 95-percent alcohol.
- C. VAN GIESON STAIN²⁴**
- Solutions*
- I. Weigert's hematoxylin
- | SOLUTION A | |
|------------------------|-----------|
| Hematoxylin | 1.0 gm. |
| Alcohol absolute | 100.0 cc. |
- | SOLUTION B | |
|---|----------|
| Iron chloride (29-percent aqueous solution) | 4.0 cc. |
| Water distilled | 95.0 cc. |
| Hydrochloric acid | 1.0 cc. |
| For use mix equal volumes of solutions A and B | |
- II. Alcoholic picric-acid solution
Water distilled 250.0 cc.
Alcohol (95-percent) 250.0 cc.
Picric acid 2.5 gm.
 - III. van Gieson Stain
Picric acid (saturated aqueous solution) 100.0 cc.
Glycerine 10.0 cc.
Acid fuchsin (1-percent solution) 5.0 cc.
Nitric acid 0.5 cc.
(or glacial acetic acid 0.75 cc.)
- Staining Method*
1. Bring sections to water as usual.
 2. Stain sections 10 minutes in Weigert's hematoxylin.
 3. Wash two times in 95-percent alcohol.
 4. Stain in alcoholic picric acid solution 30 seconds.
 5. Place sections in tap water until blue (five to 10 minutes).
 6. Stain in van Gieson stain three minutes.
 7. Dip in 80-percent alcohol.
 8. Dehydrate by three changes of 95-percent alcohol for two minutes each.
 9. Place in cedar oil for two to three minutes.
 10. Clear with three changes of toluene for about two minutes each.
 11. Mount in Canada balsam.
- RESULTS**
- A. TOLUIDINE BLUE METHOD**
- Although metachromasia is not truly specific its appearance as demonstrated by this

technique is considered evidence of the presence of activated mucopolysaccharides in the ground substance.⁸ In limbal incisions on monkey eyes there was no change in metachromasia until the third postoperative day when small scattered clumps of purple-staining matter appeared in the subconjunctival tissue. At this time there was little change in the staining properties of the corneoscleral incision.

Five days after operation fine red granules could be observed in the stroma near the edges of the wound. These granules, which were seen best with very high magnification, were more plentiful on the scleral than on the corneal side of the incision and were visible until the 10th day.

On the seventh day the subconjunctival areas of metachromasia had disappeared and large mononuclear cells filled the anterior half of the wound. In these areas metachromasia could be seen in close proximity to the cells.

By the 10th or 14th postoperative day the cells and metachromatic substance extended to the posterior end of the wound and the immediate edges of the anterior part of the incision showed some lessening in metachromasia (fig. 1). From the fifth to 10th day the scleral side of the incision often seemed to be more strongly metachromatic than the corneal part.

When an incision was made in the central cornea the reaction was quite different. There was no change until 24 hours after injury at which time the edges of the incision showed a definite loss of metachromasia in a triangular area based at Descemet's membrane (fig. 2). After five days strongly metachromatic material was present in the anterior part of the incision in the midst of this ametachromatic tissue.

B. WILDER'S SILVER CARBONATE METHOD

This silver impregnation stain demonstrates the presence of reticulin fibers in connective tissue. Thirty-six hours after operation, no fibers were seen in either subconjunctival or corneal tissues; and at the

end of three days, a time when polymorphonuclear infiltration is a prominent characteristic of the healing wound, only rare reticulin fibers were present in the subconjunctival tissue.

These fibers increased in number during the fourth postoperative day but not until the fifth day was reticulin present in the anterior half of the incision. The number of fibers varied greatly, and first appeared not at the actual wound edges, but slightly away from them. Fibroblasts or large mononuclear cells were plentiful at sites where newly formed fibers were found. During the next two days the reticulin content increased and fibers extended throughout the wound (fig. 3).

By the seventh postoperative day reticulin fibers tended to be aligned more or less parallel to the direction of the incision. In the course of the next week there was a gradual decrease in the number of reticulin fibers, and by the end of the second week after operation few if any fibers were seen except in the posterior third of the wound. When there had been excessive trauma (that is, crushing) at the time of operation or when there was gaping of the posterior lips of the wound, the appearance of reticulin fibers was delayed.

C. VAN GIESON METHOD

With this technique young collagen fibers stain yellow but as they develop the color changes first to pink and finally to red when maturity is reached. In limbal wounds there was no evidence of collagen formation for the first four days after operation.

On or about the fifth day occasional traces of immature collagen were observed around blood vessels in the subconjunctival tissue. By the seventh day yellow-staining collagen was present in all eyes but varied greatly in amount not only from eye to eye but also from section to section in the same eye.

On the 10th or 11th postoperative day there was new collagen formation throughout the wound (fig. 4). It was especially plentiful in the anterior stroma, where a

transition in staining reaction from yellow to pink was seen. During the next two or three weeks the collagen in the anterior layers became more pink in color while that in the deeper stroma still stained yellow. Not until the end of four weeks did the posterior part of the wound begin to assume a pink color. By this time the anterior stroma stained a deep pink or red but in no instance was the color as strong as that of uninjured tissue. This delay in appearance of collagen in the posterior part of the wound was a consistent finding.

In some sections no new collagen could be seen in the deeper layers as late as 11 days after operation. This slowness in formation of collagen seemed to be marked in wounds showing posterior gaping without tissue incarceration. If, however, the iris had become caught in such a wound the rate of development of collagen appeared to be equal to, if not greater than normal.

DISCUSSION

For many years biochemists have recognized the importance of enzyme systems in initiating reparative processes. In 1937 Valy Menkin studying the mechanisms of inflammation reported the isolation from inflammatory exudates of a polypeptide which attracted polymorphonuclear cells to the site of injury.³³⁻³⁴ He called this substance leukotaxin. Subsequent studies have indicated that this material, although having many properties characteristic of the chemotactic substances liberated by damaged tissue, is not the only one concerned in the response to injury.³⁵⁻³⁸ The current trend of thought is that initial reactions take place through the catalytic influences of proteolytic enzymes released within the first few hours after operation.³⁹⁻⁴³

Weimar has made some interesting observations on the initial steps in ocular wound healing.⁴⁴ She has found in the rat polymorphonuclear cells begin to invade the incised cornea during the fourth hour after operation, reach their maximum between the

24th and 36th hour, and return to normal by the sixth day. However, when sodium salicylate is applied topically to the injured cornea during the second postoperative hour this polymorphonuclear infiltration is inhibited, but if the drug is used at a later time it is ineffective. She has also found soybean trypsin inhibitor has a similar effect when applied topically either during the second postoperative hour alone or during the third and fourth or the fifth and sixth postoperative hours. Her ability to inhibit polymorphonuclear invasion by early topical application of these substances has led her to believe the machinery of repair is already in motion by the second hour after wounding. Furthermore, from these and other studies she has postulated the initial response to tissue injury is the liberation of a proteolytic substance.⁴⁵ This agent activates a chemotactic substance (a polypeptide) which in turn attracts polymorphonuclear leukocytes.

During the first few postoperative days both polymorphonuclear cells and macrophages appear within the area of the wound.⁴⁶⁻⁴⁹ We have learned to recognize them not only as scavengers but also as cells which play a more positive role in healing. The polymorphonuclear leukocytes liberate proteolytic enzymes and cause the process of repair to move forward while the macrophages may act as precursors of fibroblasts.⁵⁰⁻⁵⁹ This tissue activity so progresses that by the third or fourth postoperative day ground substance is altered and fibroblasts appear in the wounded area.

There is no unanimity of opinion concerning the time at which metachromasia of the ground substance is first observed. Sylvén found changes adjacent to blood vessels as early as 24 hours after operation, and by 72 hours metachromasia had become well established within the healing wound.¹⁷ Campani and Reggianini studying skin incisions in dogs described "heaped-up areas" of metachromasia scattered throughout the ground substance in 48- to 96-hour wounds.⁶⁰

Perez-Tamayo and Ihnen⁶¹ have reported

strongly metachromatic material in skin wounds in rats two days after operation; while Pirani, Stepto, and Sutherland,²³ studying the healing of laparotomy wounds in guinea pigs, observed increasing metachromasia of the ground substance from the second to the 12th postoperative day.

These differences may well be caused by individual variations in interpretation or in the very delicate staining techniques required to demonstrate metachromasia. Be that as it may, investigators agree metachromasia first is seen in the vicinity of blood vessels and in areas where fibroblasts show signs of increased activity.

Observations upon metachromasia in ground substance of corneal incisions have been made by Aurell and Smelser.^{62, 63} In 1954, the former investigator described changes in metachromatic staining during the healing period. For these studies he made perforating linear incisions on rabbits' corneas and killed the animals at various intervals after operation. The corneal wounds were stained with toluidine blue and examined histologically for the presence of the metachromatic substance (mucopolysaccharide) in the corneal scar. At the end of 24 hours no change in staining reaction was noted except that caused by swelling of the wound edges, but after six days the scar had become markedly metachromatic. He believes this increase in metachromasia in the wound closely parallels the formation of collagen fibers. To substantiate this opinion he demonstrated marked metachromasia at the end of two weeks and a gradual decrease in this staining reaction as the healing progressed. Ultimately the scar showed slightly less metachromasia than did the normal cornea.

Aurell thinks the newly formed fibrils, by maintaining their metachromasia, are "closely related genuine corneal fibrils," but Rycroft points out that they differ both in character and composition from those normally present in corneal stroma.⁶²

Smelser (in an unpublished experiment)

has studied the healing of corneal incisions on rabbits. The animals were killed at two, seven, 10, 15, and 22 days after operation and the wounds sectioned and stained either with hematoxylin and eosin or with toluidine blue. At the end of 24 hours this investigator found a triangular zone based toward Descemet's membrane in which there was no metachromasia. On either side there was a gradual transition to normally metachromatic stroma. After seven days an area of increased metachromasia occurred along the edges of the anterior part of the wound and gradually extended toward the posterior corneal surface. At the same time it spread laterally to cover the previously ametachromatic area.

Both Smelser and we have observed the early appearance of metachromasia in the area containing fibroblasts and where collagen will first be seen. This correlates well with Dunphy and Udupa's theory that collagen is formed by an interaction between a protein product of fibroblasts and components present in activated ground substance.³

The significance of the ametachromatic period in a previously metachromatic cornea is difficult to explain. François and Rabaey studying in rabbits the response to corneal injury and inflammation have suggested that loss of metachromasia occurs when edema of the corneal stroma causes a decrease in unit volume concentration of the corneal mucopolysaccharides without actually diminishing the total mucopolysaccharide content.^{28, 29} This hypothesis may explain the immediate loss of corneal metachromasia after injury but it is difficult to reconcile it with the persistent absence of such staining reaction to new strongly metachromatic tissue. It would seem more plausible that the processes of repair lead to a definite change in the properties of the corneal mucopolysaccharides.

As metachromasia of the ground substance develops, reticulin may be demonstrated in the same areas. This substance is considered

by many investigators to be a precursor of collagen fibers.^{3, 6-8} Sylvén has described precollagenous silver-staining fibers appearing in strongly metachromatic areas on the fourth postoperative day and many observers have noticed that reticulin decreases as collagen increases in the wounded area.^{3, 17}

Our observations are in accord with those investigators who have demonstrated reticulin relatively early in the course of healing at a site where collagen later appears. Thus, both reticulin and collagen are first seen near subconjunctival blood vessels, then appear in the anterior part of the wound, and finally along its posterior edges. We may postulate that reticulin precedes collagen and is intimately concerned in its formation.

Numerous investigators have noted that these two substances are composed of similar building units (micro-fibrils) although their staining and chemical characteristics differ greatly.^{4, 6, 7} Much interest, therefore, has centered on the use of silver impregnation stains for the demonstration of reticulin and it has been shown that silver is deposited on the fibers rather than forming a chemical composition within the fiber.⁶⁴ Tomlin has suggested that silver staining is an interface phenomenon which occurs at the fiber-ground substance boundary and may depend more upon variations of the latter than on differences in the fibers.⁶⁵ This conception substantiates the hypothesis that there is great activity both intra- and extracellularly during the early postoperative period.

In recent years many investigators have come to look upon collagen formation rather than fibroblastic proliferation as the mechanism on which the tensile strength of a wound depends.^{3, 24, 25} Dunphy and Udupa have correlated the rise in collagen content with the gain in tensile strength in abdominal wounds of rats. From these studies, those of Abercombie and his associates, and others, it has been shown that the rise in tensile strength coincides with the appearance of collagen fibers within the wound edges.^{3, 24, 26, 66} However, recent evidence suggests tensile

strength may depend not upon the collagen content of the fibers but rather upon a mucin-collagen combination which is the innermost cement substance binding together the fibrils.^{67, 68}

Although similar studies on limbal wounds have not as yet been reported, we can compare our present observations with the findings of Gliedman and Karlson.⁶⁹ These investigators using a tensiometer studied in cats the breaking point of limbal incisions made without a conjunctival flap and closed with 6-0 silk sutures. They found the immediate postoperative strength of the sutured wound to be 6.1 percent of normal and on the sixth postoperative day it was 9.9 percent rising to 34 percent by the 14th day.

This rapid increase in tensile strength occurring in the second postoperative week closely parallels our observations on the development of collagen. We found young collagen present on the seventh day after operation and by the 14th day it had become more plentiful and showed some evidence of maturing. During the next two months, the collagen fibers continued to develop but remained considerably less mature than those in normal stroma. This finding is compatible with Gliedman and Karlson's observation that at the end of 56 days the tensile strength of their limbal wounds was only 41 percent of normal.

We may inquire what agents can stimulate or delay wound healing. Howes has said that "the process may be interfered with more readily than it can be stimulated."⁷⁰ Indeed, it is doubtful if any substance has been found which actually accelerates the normal rate of healing. In contrast many compounds have been shown to delay the development of collagen. If we accept Dunphy and Udupa's theory that collagen arises from a series of reactions taking place between a protein component of fibroblasts and the mucopolysaccharides of the ground substance, it follows that collagen formation is inhibited by any agent which interferes with (1) fibroblast formation, (2) metachromasia

of ground substance, or (3) any stage in the interaction between (1) and (2).

Fischer and Bocher have demonstrated heparin inhibits the division of fibroblasts, while others have found metachromasia of ground substance is delayed by freezing or crushing the tissue to be incised.⁷¹⁻⁷⁶ Smelser (unpublished experiment) has studied the healing of an incision in an area of rabbits' cornea made acellular by freezing.⁶⁹ He found the cellular infiltration to be only slightly less in the frozen corneas than in the control eyes. The number of fibroblasts were also about equal in the two groups but there was a significant difference in the metachromatic staining reaction. In the frozen corneas the metachromasia was much less than in the control group. The freezing apparently prevented the formation of collagen by inhibiting the liberation of the mucopolysaccharides in the ground substance. In the frozen corneas Smelser noted a delay in healing of the posterior part of the incision, which lack of union he attributed to the absence of collagen.

Pirani and his co-workers studied the effect of desoxycorticosterone acetate upon the healing of abdominal wounds in guinea pigs.²³ They described an active proliferation of fibroblasts and an increased metachromasia of ground substance but the appearance of collagen was delayed and the amount formed less than normal. Lattes and his associates, and many others, have investigated the action of cortisone upon wound healing in rats.⁷⁷ They found the delay in tissue healing was not apparent immediately following injury, but after two to four days there was a depression of all new connective tissue elements and especially a reduction in the metachromasia of the ground substance. Similarly, Udupa, Waessner, and Dunphy have shown the accumulation of mucopolysaccharides is depressed and collagen formation retarded when the amino acid, methionine, is removed from a guinea pig's diet.⁷⁸ There is some similarity between these effects and those occurring in scorbutic guinea

pigs.^{19-25, 79-81} In this condition the tissues show a lowered tensile strength, the ground substance is highly depolymerized, and wound healing is delayed.

CONCLUSIONS

Based on the histologic appearance and changes in tensile strength, wound healing has been divided into three phases: (1) lag phase, (2) fibroblastic phase, and (3) cicatricial phase.

In view of more recent studies certain modifications in this theory can be postulated. For instance we now know that activity begins almost immediately after the infliction of a wound.

There is no uniform agreement on the exact nature of the early changes but most authorities look upon the liberation of a chemotactic substance (a polypeptide) from the injured cells as the initial step. This chemotactic agent sets in motion a chain of reactions of which we know very little. However, as a consequence polymorphonuclear leukocytes appear, proteolytic enzymes are activated, and lymphocytes, macrophages, and fibroblasts appear in the injured area. In the presence of young fibroblasts or mast cells the mucopolysaccharides of the ground substance become activated.

By a series of complex reactions between a protein component produced by fibroblasts and the mucopolysaccharides, a procollagen, reticulinelike in nature, and finally collagen are formed. With the appearance of collagen, the tensile strength of the wound increases and, as the collagen fibers mature, approaches that of uninjured tissue.

In the light of these newer facts the suggestion of Dunphy and Udupa that wound repair can be divided into two stages seems plausible. These authors have separated the periods into (1) the productive or substrate phase lasting from the first to fifth day and (2) the collagen phase which extends from the fifth day until healing is complete.

During this first period the foundations of repair are laid down without any material

gain in the tensile strength of the wound, while the predominant features of the second phase are the formation of collagen and a consequent increase in tensile strength.

These stages of wound healing have been observed in corneal and in limbal wounds. Because of the avascularity of these tissues healing is somewhat slower than that reported in skin wounds. Owing to the transitional nature of the limbal tissues metachromasia of its ground substance presents a complex pattern unlike that reported in other tissues.

SUMMARY

The healing of corneal and limbal wounds has been studied using differential histologic staining methods. The findings have been correlated with recent ideas about wound repair. The results support the modern concept of great tissue activity during the first few days after operation.

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EXUDATIVE RETINAL DETACHMENT*

A REVIEW OF THE LITERATURE AND REPORT OF A CASE

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Retinal detachments are commonly classified as spontaneous or idiopathic, or as secondary. This classification is primarily a clinical one, based on whether the clinician can discover some overt cause for the detachment or whether it appears to occur with no underlying basis. Actually, the difference between the two is probably a matter of degree rather than type and all are probably secondary to some degenerative, inflammatory, or neoplastic changes. At the present time those detachments that occur along with or following chorioretinitis, gross uveitis, scleritis, episcleritis, hemorrhagic lesions, intraocular tumors, trauma, and any other inflammatory lesion which may cause changes in the choroidal circulation may be considered as secondary while all others are termed spontaneous or idiopathic.

A second classification, which supplements that just described is based on the type of subretinal fluid found under the detachment; this may be exudative or serous.

The exudative type is essentially due to a vascular disturbance in the choroid, caused either by inflammation or engorgement or both. Stasis in the choroidal circulation leads to an upset in the pressure equilibrium of the eye and allows an exudate to form under the retina.

The second and more common type in this classification is the serous type which is essentially due to local inflammatory conditions of chorioretinitis, degenerative changes, or trauma. In this type there is always presumed to be a retinal tear or hole.

It is interesting to note that the exudative theory was the first one advanced to ex-

plain all retinal detachments and was commonly accepted in the early pre-ophthalmoscopic era. Pathologic studies, although rare, have confirmed the existence of these two types.

Some cases are associated with an advanced vascular disease of the choroid and an albuminous subretinal fluid of an exudative type. In these cases the retina has shown very little histologic alteration even after considerable time has elapsed, but the choroid is characterized by very marked degenerative changes. In these cases the obvious cause of the detachment would seem to be the accumulation of a subretinal edema from the choroidal capillaries.

A majority of cases which have been studied, however, show changes in the retina only and the subretinal fluid is of a serous type. In these cases the most characteristic feature is the occurrence of one or more retinal holes. The subretinal fluid in these cases is usually relatively clear and non-coagulable, resembling vitreous fluid but with a higher content of albumin and a variable content of chloride. The most commonly accepted theory of this fluid's origin is that it is derived from the vitreous and has percolated through the retinal hole.

The literature is voluminous on the serous type of detachment with speculations as to etiology and suggestions for management. However, in current literature there are fewer references to the exudative types of detachment. The purpose of this paper is to review some of the causes of exudative detachments and to report a case of bilateral detachment with spontaneous re-attachment which falls into this category.

According to Duke-Elder¹ the exudative mechanism is clearly responsible in certain

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Fig. 1 (Lewallen). Proptosis and chemosis accompanied by exudative retinal detachment.

types of detachments which may be secondary or spontaneous. These are those which are associated with a passive congestion of the choroid and those caused by transudation from the vessels, such as is typified by renal retinopathy. In these cases the fluid is highly albuminous and may coagulate.

The sequence of events involves a stasis in the choroidal circulation, a raising of capillary pressure in the choriocapillaris, a dilation of the small vessels with an increased permeability of their walls, and the exudation therefrom of a protein-rich transudate which collects in the potential space of the primary optic vesicle and thus elevates the retina. This entails a disturbance of the pressure equilibrium on either side of the retina; and once a colloid-rich fluid starts to collect in this space, being of a high osmotic pressure and surrounded by membranes which are impermeable to colloids but permeable to water, it tends to augment in bulk by the osmosis of fluid from the vitreous.

This type of detachment has been relatively easy to produce in rabbit eyes. Any insult which produces an exudative choroiditis will produce an exudative detachment of the retina if the stimulus is severe enough. Such a condition has been produced by subconjunctival injections, episcleral injections, by injections between the sclera and choroid, and by cauterization of the sclera. Most of these detachments have subsided spontaneously, if given enough time, unless gross hemorrhage and/or vitreous changes occur. A similar effect results from the stasis and

edema produced by ligation of the optic nerve.

Among the causes of exudative detachment discussed briefly in modern textbooks of ophthalmology are renal retinopathy and the toxic retinopathy of pregnancy. According to Duke-Elder, detachment occurs in about five percent of cases of renal retinopathy. He states that it is relatively common in toxic retinopathy of pregnancy, frequently occurring bilaterally. Foster-Moore is quoted as saying that 60 percent of pregnant cases recover spontaneously while only 15 percent of nonpregnant ones may be expected to recover spontaneously.

The first reported case of toxic retinopathy of pregnancy with detachment was by von Graefe in 1855 and since then a considerable number have been recorded. Schiøtz collected 50 cases in 1921, and Fry, in 1929, reported a total of 57 cases. There are few reports of cases in the past 10 years, perhaps largely due to the decrease in the number of complications of pregnancy.

The condition is usually associated with a generalized edema, frequently marked about the face and lids. It is invariably associated with marked retinopathic changes. The prognosis for spontaneous reattachment is good but the prognosis for vision must be guarded, as it depends on the residual damage left by the accompanying retinopathy.

In contradistinction to its frequency in pregnancy cases, detachment is relatively rare in renal retinopathy, although it may be seen more commonly than is thought as a terminal phenomenon. It is usually associated with advanced disease and generalized anasarca and is of very grave prognosis. Such detachments are usually large, globular, and bilateral, and situated in the lower part of the eye. The detachment generally resolves if the patient survives.

A massive choroidal exudate associated with generalized disease has been cited as a factor in rare cases: in malaria (Terson, 1903), rheumatism (Schreiber, 1920), and in gout (Greeff, 1929). Exposure to strong

light followed by retinal edema and detachment is cited by Harmon and Macdonald (1922) and by Rauh in 1927.

Tumors and extraocular inflammations, such as orbital cellulitis, abscess, tenonitis, scleritis, and sinusitis, which may be associated with passive congestion of the choroid, may give rise to an exudative detachment.

A proliferating retinosis occurring after hemorrhage into the vitreous may produce such a detachment, and allergy has been implicated in the explanation of bilateral exudative detachment, as in the cases reported by Balyeat¹⁷ and Prewitt.¹⁸

Harada's disease, which is a well-known syndrome, falls into this class of detachments. This condition was described in 1926 by Harada with the report of 10 cases, in which there was bilateral acute diffuse choroiditis with retinal detachment associated with neurologic disturbances. Some patients suffered impaired hearing and various skin and hair changes such as alopecia, vitiligo, and poliosis.

The onset of these cases is usually sudden—patients complain of headache, nausea, vomiting, and there is usually notable impairment of vision, sometimes progressing to bare light perception within a few days. In the early stages opacities of the vitreous and edema of the disc suggestive of papillitis are present. Detachment may progress to complete but usually subsides within a few weeks, with restoration of normal vision. The fundus usually shows depigmented areas and white patches in the periphery which are suggestive of sympathetic choroiditis.

This syndrome appears to be closely related to that described by Vogt and Koyanagi except that detachment is not a rule in all reported cases of Vogt-Koyanagi syndrome. Recently Cowper² and also Hogan³ have advanced the theory that Harada's and Vogt-Koyanagi syndromes are manifestations of the same disease and Duke-Elder¹ also states that they may be related etiologically, with Harada's representing a milder form of the disease. Cowper proposed that

the term "uveoencephalitis" be substituted for both of these terms. The etiology of either of these syndromes has not been defined but research work, chiefly by Japanese workers, has strongly suggested a viral etiology in both cases.

Knapp,⁵ in 1944, reported 16 cases of serous retinal detachments in which reattachment had occurred spontaneously and described the ophthalmoscopic picture. According to him the picture in these cases is rather distinctive and should not be confused with the appearance of the fundus following an exudative detachment.

In the serous type following reattachment the retina gradually changes to a pale yellow-gray with characteristic branching white lines (subretinal) and areas where choroidal markings are more distinct and irregular retinal pigmentation is present.

The upper boundary consists of organized exudate which extends across the fundus below the disc in a curved or more or less straight line to the periphery on each side and divides the fundus into two dissimilar parts. This boundary limits the extent of the detachment unless the limiting line does not extend clear to the periphery, in which case a new detachment may develop.

In each of Knapp's cases the detachment was old and there were retinal holes or dialyses in nine cases. By contrast the ophthalmoscopic picture in the exudative type of detachment is normal or almost so, except in the inflammatory cases such as Harada's syndrome, and holes in the retina are never seen.

Forbes⁶ reported a case of spontaneous reattachment in a patient treated with aureomycin. His patient was a young man in whom there had been a successful surgical reattachment below some three months prior to the occurrence of the detachment above. This patient had positive Mantoux and brucellosis skin tests.

The entire upper half of the retina was detached, with vitreous floaters. Besides aureomycin the patient was treated only by

pinhole glasses but was not put to bed. Eighteen days later there was complete reattachment. It would seem likely that this case was of the exudative variety; the etiology was undetermined with speculation that brucellosis or tuberculosis might have played some part.

Three cases of exudative detachment, in two of which there were spontaneous reattachments, have been reported as complications of herpes zoster ophthalmicus.¹⁰ In the third case, a peripheral hole was found and the eye operated. In all of these cases an anterior uveitis was present and in one case a severe posterior uveitis.

Inflammatory changes of a sclerotic nature have long been known to cause exudative detachments. Dustacher, in 1891, first observed a case of scleritis complicated by separation of the retina with spontaneous healing, and a similar case was reported by Kamocki⁸ in 1892. In each case the condition was unilateral. Dustacher's patient also had uveitis. Separation of the retina took place in an area corresponding to the scleral pathologic process and, according to the explanation of Dustacher, was due to the disturbance of lymph circulation following infiltration of the sclera.

Leber⁹ in his work on retinal disease, mentioned retinal separation in the course of scleritis and episcleritis and tried to explain the mechanism as being similar to that in cases of phlegmon of the orbit in which infiltration proceeds along the emissaries to the inner membranes of the eye.

Horay¹⁰ and Csillag¹¹ have also reported cases which appear to belong in this category. Csillag had a patient with marked scleritis in the upper part of the sclera, ciliary congestion, hyperemic disc, no uveitis, and a detachment in the upper nasal quadrant without holes. The detachment progressed and, in the course of the disease, the lower and temporal parts separated too, accompanied by exophthalmos, chemosis of the conjunctiva, and exudation in the retina, finally enveloping the retina. The condition re-

mained unilateral and cleared spontaneously. The explanation given was that the acute inflammatory reaction caused edema of the choroid, the stasis of tissue fluids sank downward, due to the loose consistency of the choroidal structures, and the increased volume resulted in detachment of the retina. After subsidence of the condition the fundus revealed no pathologic changes referable to the previous choroidal inflammation.

Horay's patient developed a scleral nodule in the right eye and later chemosis of the conjunctiva, periosteal irritation temporally, and a temporal detachment. Later, visible exophthalmos developed with total retinal detachment. The detachment subsided in time with conservative treatment.

Karasek¹² reported a case of deep scleritis with retrobulbar neuritis, paresis of the abducens, and a flat detachment in the macular region which was explained by exudation between the sclera and choroid with ensuing inflammatory involvement of the choroid and retina.

Meisner¹³ reported four cases in this category which occurred among 150 cases of detachment. One was a case with evidence of choroiditis and a positive tuberculin test; one was a case of painful scleritis of many months' duration and the other two were cases accompanying iridocyclitis. Three were unilateral but one occurring with uveitis was bilateral. In all cases conservative therapy resulted in reattachment.

REPORT OF A CASE

L. S., a 103-year-old Negro was admitted to the orthopedic service of the Jefferson Davis Hospital on July 12, 1954, because of a chronic draining osteomyelitis of the right ankle which had failed to heal on conservative therapy for about one year.

Physical examination on admission revealed a blood pressure of 190/100 mm. Hg. A few carious teeth were present. There was a large cystic mass on the left posterolateral surface of the neck, soft and nontender. The patient stated that this had been present

since a bayonet wound in 1865. There was edema below the right midtibial area with one draining ulcer over each malleolus. The entire right foot was tender and swollen.

Eye examination showed normal pupillary reaction, marked arcus senilis, and "normal fundi."

The eye service was first called in consultation on July 19, 1954, because of "chemosis of the right eye." The patient stated that the right eye had begun to swell about four days before with some pain. He had noted no diminution in vision.

Examination revealed marked proptosis and chemosis of the right eye with a scanty conjunctival exudate. There was moderate injection of the swollen conjunctiva and the cornea was slightly cloudy. The anterior chamber appeared clear. The pupil was small and reacted sluggishly to light. The patient could count fingers accurately at six feet.

Tension was: O.D., 28 mm. Hg; O.S., 19 mm. Hg (Schiotz). With a Hertel exophthalmometer the right eye measured 29 and the left 21. Pupils were dilated with 10-percent neosynephrine; both dilated well.

Ophthalmoscopy revealed a normal appearing disc and vessels with a retinal detachment nasally and temporally and extending to within two disc diameters of the disc on either side. No holes or disinsertions could be seen on repeated careful examinations. A preliminary diagnosis of proptosis and chemosis due to orbital cellulitis or tumor with a secondary retinal detachment was made.

X-ray films of the orbit, skull, sinuses, and chest were reported as negative. A complete skeletal survey was negative for any evidence of a generalized disease. Otolaryngologic consultation reported no abnormalities in the nose or sinuses.

Serology was negative. Wbc was 5,420 with a normal differential. Hemoglobin was 10.3 gm. Urine was reported as normal and a culture from the right eye was reported as negative for pathogens. Culture from the draining sinuses of the right ankle revealed

Staphylococcus aureus, which was hemolytic, *Proteus*, and *Escherichia coli*.

Because of the possibility of metastatic orbital cellulitis or abscess, the patient was placed on heavy doses of antibiotics, including penicillin, streptomycin, and a triple sulfa preparation. The right foot and ankle were amputated above the malleoli on July 20, 1954.

On July 22nd, the detachment was almost complete, extending from the 2-o'clock around to the 10-o'clock position, and almost to the disc on all sides. The left eye remained normal.

On July 28th, there was much less chemosis, the patient being able to close his lids. The retina remained elevated but appeared less so. On August 4, 1954, there was no edema or chemosis of the right eye and the retina appeared completely reattached in all areas. Beginning edema of the conjunctiva of the left eye was noted. On August 6th, there was marked proptosis and chemosis of the left eye and the retina, O.S., was completely detached. The retina in the right eye remained flat and vision in the right eye was now 20/70. Hertel exophthalmometer readings were 20, O.D., and 28, O.S.

Antibiotics were continued. A sternal aspiration biopsy was attempted but no marrow could be obtained. The Wbc remained normal and the patient was afebrile. A skin test using the Frei antigen was negative. The patient was placed on Diamox (250 mg. every six hours) and a low salt diet.

On August 20th the edema and proptosis were subsiding and the retina was seen to be flattening out except inferiorly. By August 27th, all the chemosis and edema had subsided and the retina was flat except for an area inferiorly where it remained elevated six to eight diopters. Hertel exophthalmometer readings were 23.5, O.D., and 23, O.S. The retina, O.D., remained flat. Vision was 20/70, O.D., and 20/200, O.S. (illiterate chart). Tension was: O.D., 19.9 mm. Hg; O.S., 17.5 mm. Hg (Schiotz).

The patient was dismissed from the hos-

pital on September 18, 1954, and followed in the out-patient clinic. Because of his advanced age and difficulty in ambulation he did not return to the clinic with any degree of regularity. He was seen again, however, on December 31, 1954, at which time vision remained as already given. After dilation, the retina in each eye was found to be completely flat with no evidence that he had ever had a detachment. Tension was normal, O.U., and exophthalmometer readings were 23.5, O.D., and 22.5, O.S.

DISCUSSION

This case is of interest from several aspects. As stated earlier, there are few recent reports of exudative detachments and it is my impression that they are rather rare. A review of the literature revealed no comparable case where an identical process involved both eyes in sequence.

The exact etiology of this case remains open to speculation although the mechanism of the detachment would seem rather clear. The orbital process which was responsible for the chemosis and proptosis caused an accompanying congestion of the choroid by stasis, with a resulting exudation of fluid in the subchoroidal space and a subsequent retinal detachment.

The etiology of a metastatic orbital cellulitis would be more acceptable if the patient had exhibited greater signs of infection, that is, he showed no leukocytosis or febrile response and he did not at any time appear acutely ill, as might be expected with an orbital cellulitis or abscess. However, the long-standing infection in his leg, plus his advanced age, might account for the inability of his leukopoietic and thermoregulatory systems to show a proper response. In view of the absence of other positive findings, orbital cellulitis would seem to remain as the most likely etiologic possibility.

SUMMARY

The literature on exudative retinal detachment is reviewed, the mechanism of exudative detachment is presented, and some of the causes are discussed. It is possible that more cases of this nature might be seen if fundusoscopic examinations are carefully made in more cases of systemic illnesses.

A case is presented in which there were in sequence bilateral exudative detachments secondary to orbital cellulitis, with complete reattachment in each eye.

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OBSERVATIONS ON THE PATHOLOGY OF RETINAL DETACHMENT OPERATIONS ON HUMAN EYES*

PART I. DIATHERMY REATTACHMENT

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The Eye Pathology Laboratory at Stanford University Hospitals has accumulated over the past 15 years a number of eyes of patients who have undergone retinal detachment surgery. Some of these eyes were enucleated while the patient was alive; others were obtained at autopsy when the patient died from other causes.

The literature contains very few reports of the pathology and histology of retinal detachment operations performed on human eyes. For this reason this paper was undertaken at the suggestion of Dr. A. E. Maumenee when he was director of the Division of Ophthalmology at the Stanford University School of Medicine.

Included in this and a subsequent paper are specimens of diathermy reattachment operations, penetrating scleral resections, and lamellar scleral resections. Observations will be made, rather than conclusions drawn, for a number of reasons. First, the number of specimens is relatively small. Second, although relatively standard techniques were employed, there may have been slight variations in procedure from case to case, as well as differences in the condition of the

various eyes to begin with. Third, many of these specimens are examples of unsuccessful attempts at reattachment. The post-operative pathologic findings might be somewhat different in successful cases. Nevertheless, there are a number of interesting, and possibly clinically valuable, observations that can be made from this material.

The techniques of operation employed were essentially those described by Pischel¹ (diathermy), Pischel and Kronfeld² (penetrating scleral resection), and Berliner³ (lamellar scleral resections). Major deviations from these techniques will be mentioned where necessary.

This paper will deal with diathermy reattachment operations. A subsequent paper will take up scleral resection procedures.

The effect of diathermy on the coats of the eyeball has been comprehensively studied by Pischel⁴ and more recently by Scheie and Jerome,⁵ Wadsworth,⁶ and Swan and Christenson.⁷ Among the factors influencing the tissue changes are the intensity, duration, and type of current, length, type, and insulation of the electrode, thickness of the sclera, and dryness of the field.

In our series, the major factor determining the appearance of the ocular tissues, particularly the sclera, after diathermy was the time that elapsed between the operation and enucleation. Pischel's partially penetrating

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Fig. 1 (Tamler). Gross appearance of the inside of an eye six days after operation.

electrode was used in all of the following cases.

Figure 1 shows the gross appearance of the inside of an eye six days after diathermy retinal reattachment operation. The patient was a 64-year-old man who had a retinal detachment of two weeks' duration. Examination at the time of operation revealed 13 separate breaks temporally and above. Six days postoperatively the patient died of a coronary occlusion.

In the figure of the vertically cut eye the round spots that look like the suckers of the

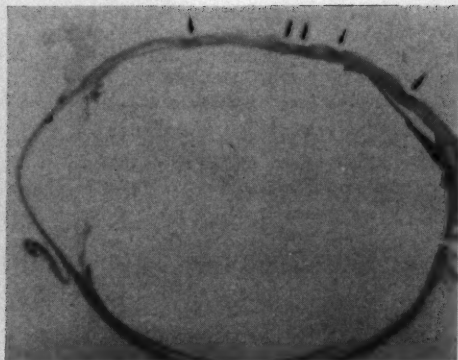


Fig. 2 (Tamler). Section of eye in Figure 1. The retina is well apposed to the wall of the globe.

tentacles of an octopus are areas of chorioretinitis corresponding to the diathermy applications to the sclera. Figures 2 to 6 are sections from this eye.

In Figure 2 the retina is well apposed to the wall of the globe except for the macula, indicating that a successful result is possible in spite of the many retinal holes. Arrows point to sites of diathermy applications. Note the flattening of the superior sclera by the diathermy, as previously reported by Wadsworth.⁶

Figure 3 shows a retinal hole sealed off by diathermy chorioretinitis. The chorioretini-

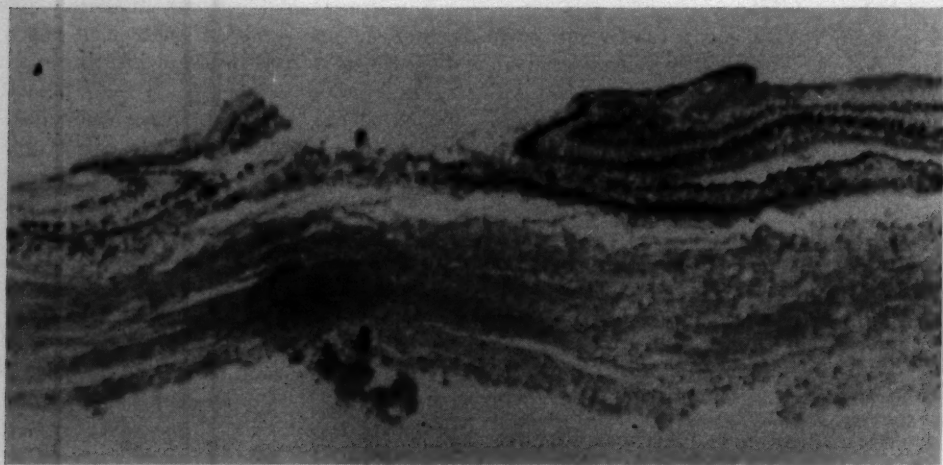


Fig. 3 (Tamler). Section of eye in Figure 1. A sealed-off retinal hole.

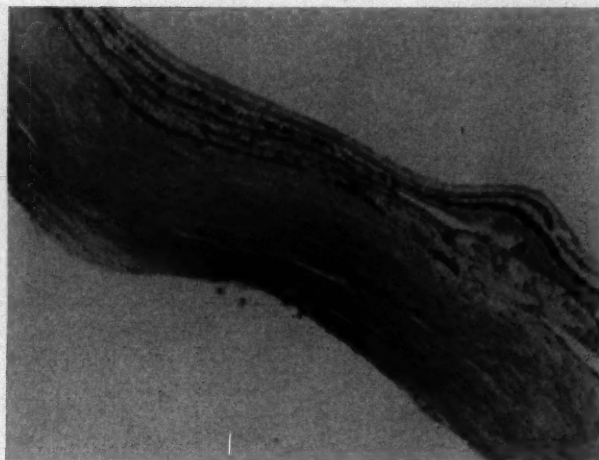


Fig. 4 (Tamler). High-power view of diathermy site of eye in Figure 1.

tis extends laterally beyond the borders of the hole and involves the adjacent attached retina.

Figures 4 and 5 show higher-power views of diathermy sites. In this relatively fresh specimen the involved sclera is shrunken and acellular. Underlying the sclera there is early chorioretinitis including a subretinal fibrin-

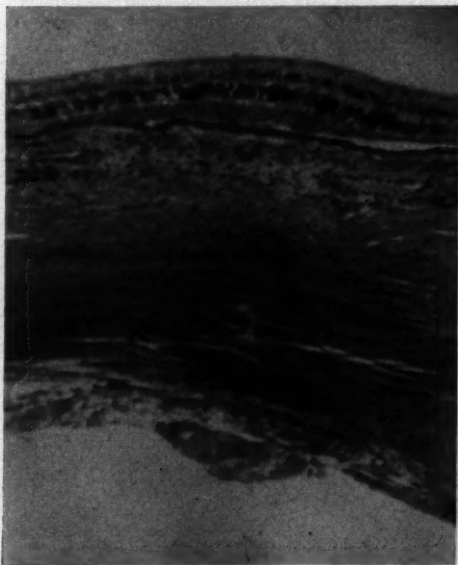


Fig. 5 (Tamler). High-power view of diathermy site in eye in Figure 1.

ous exudative coagulum. Notice that the shape of the area of scleral reaction is that of a wedge or triangle with the wide base on the scleral surface.

Next to the choroid the apex of the reaction is much narrower. At first glance this would suggest that we should put our diathermy applications one right next to the other so that the tips of the reaction are close together at choroidal depth. However, Pischel⁴ has shown, and the figures bear this out, that the inflammatory reaction in the choroid spreads laterally. In fact in Figure 4 it has extended on the left side to the region of the next diathermy application. Swan and Christenson⁷ suggest that this spread may be due to spread of the diathermy heat by the vascular system of the choroid.

Figure 6 shows the track of a partially penetrating electrode. It is filled with a plug of loose tissue containing fibrin, fibroblasts, and a few acute and chronic inflammatory cells. It is probably such a plug of tissue that was found by Pischel and Kronfeld² to be of cheesy consistency grossly and which could be picked out with a forceps when they re-operated cases which had recently had diathermy.

The healing of the scleral wound appears to proceed mainly from the episclera. This is



Fig. 6 (Tamler). Track of partially penetrating electrode. (Eye in Figure 1.)

in accord with the observations of Pischel,⁴ Weekers,⁸ and Scheie and Jerome.⁹

After the acute stage of fresh diathermy, and with the lapse of time and progression of scleral healing, the tissues present a somewhat variable histologic picture in this series. Figure 7 shows an area of diathermy in an eye of a patient who died 12 days post-operatively from a myocardial infarction. The sclera shows minimal reaction, whereas the episclera is greatly thickened by inflammatory and connective tissue. There is evidence of a diffuse but moderate chorioretinitis.

Figure 8 is a section from the periphery of an eye of a 68-year-old man who suddenly died of a pulmonary artery embolus 19 days after a diathermy reattachment procedure. There is heavy episcleral reaction. The sclera is still somewhat acellular and

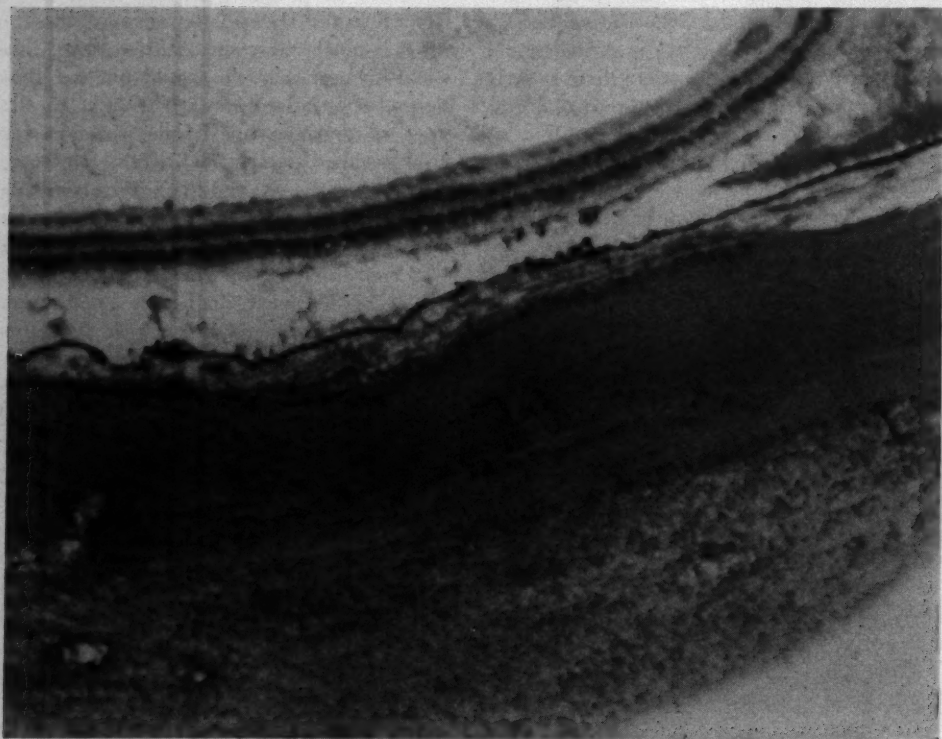


Fig. 7 (Tamler). Area of diathermy in an eye of a patient who died 12 days after operation.

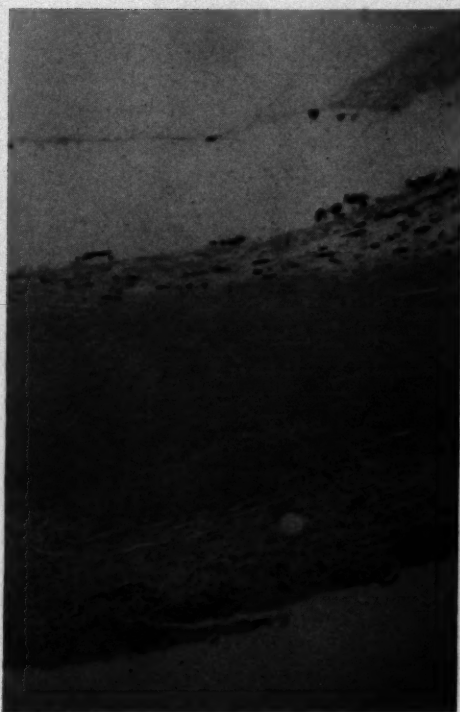


Fig. 8 (Tamler). Section from the periphery of an eye of a 68-year-old man who died 19 days after operation.

there is some disruption in the arrangement of its fibers. The choroidal architecture is distorted and there is much pigment clumping in the choroidal stroma. The pigment clinging to the inner surface of the choroid and outer surface of the retina suggests chorioretinal adhesions that were broken in the preparation of the slide. Note the variable thickness of the retina. In the center of this section the retina consists of a single fiber layer. This section was taken near the ora serrata.

Figure 9 shows pigment proliferation in a diathermy scar in an eye enucleated 14 months after a detachment operation. There is increased cellularity of the sclera.

In Figure 10 is shown a diathermy site in the eye of a 58-year-old woman. The eye was enucleated one and one-half years after

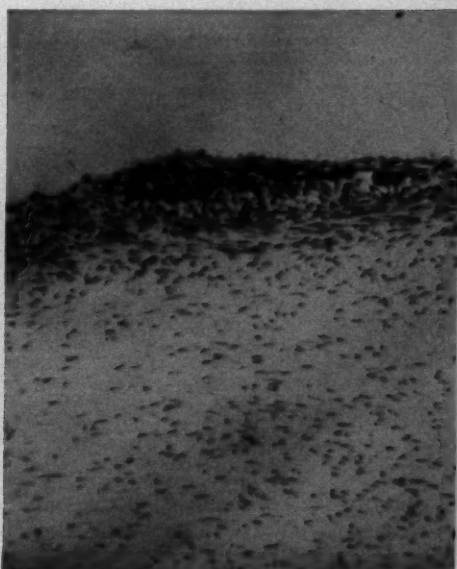


Fig. 9 (Tamler). Pigment proliferation in a diathermy scar.

an unsuccessful diathermy reattachment procedure for an aphakic detachment with multiple holes. The sclera is thickened and scarred. The choroid, too, is scarred. The pigment epithelium is degenerated and a fibrovascular membrane (arrows) lies between it and the subretinal fluid.

Thus these sections do not manifest any consistent pattern of healing in the diathermy scar. This may be due to the many variables in the use of diathermy as already mentioned.

In addition to the changes in the tissues



Fig. 10 (Tamler). Diathermy site in the eye of a 58-year-old woman.

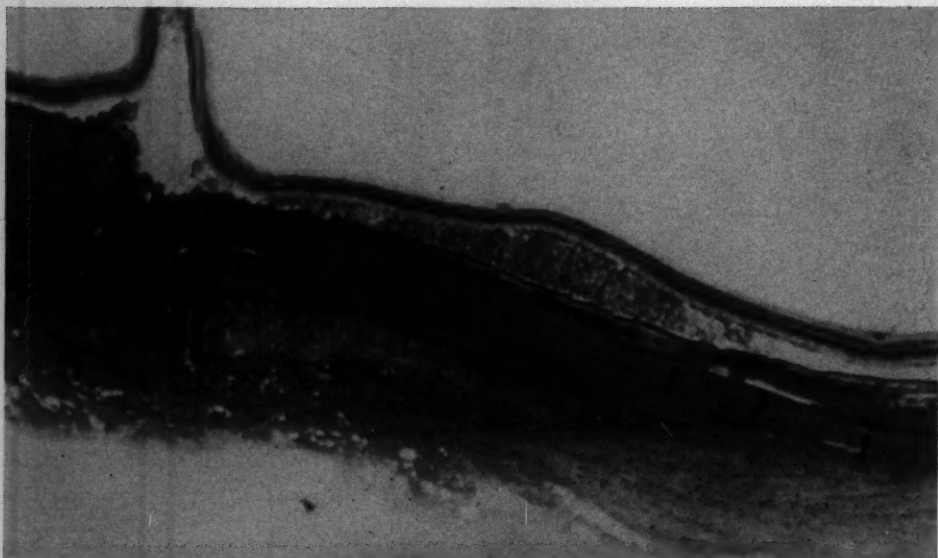


Fig. 11 (Tamler). The arrows point to the path of a vortex vein running posteriorly from the choroid through the sclera.

following diathermy, as already described, some other observations were made that may have some clinical value.

In Figure 11 the arrows point to the path of a vortex vein running *posteriorly* from the choroid through the sclera. Several authors^{2,9,10} have pointed out the serious complications that may result from diathermizing a vortex vein. From the direc-

tion of the vortex vein in Figure 11, it seems logical to apply the diathermy posterior to the exit of the vortex vein on the sclera and thereby avoid cooking it in its intrascleral course.

Two other eyes illustrate a possible and

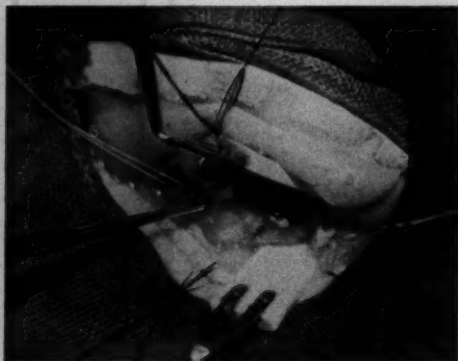


Fig. 12 (Tamler). Arrow points to a dark mass bulging through the sclera.

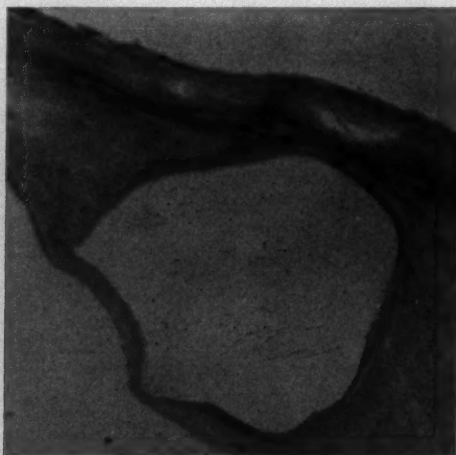


Fig. 13 (Tamler). The mass turned out to be a scleral cyst.

interesting complication of intensive diathermy treatment, namely, the formation of cysts in the wall of the globe.

The first patient was a 64-year-old man who in February, 1952, was treated elsewhere with diathermy for a detachment of the temporal retina with a horseshoe tear in the 9-o'clock meridian. Fair drainage was obtained but the pins could not be seen at the time of operation. Postoperatively, a definite hole was still seen at the 9-o'clock position and the retina remained detached. Therefore, three and one-half weeks after the original operation, a second diathermy reattachment was attempted. No drainage was obtained this time and the retina remained elevated postoperatively. Two months later the patient came to the west coast and was noted to have detachment of the temporal half of the same retina with a questionable tear at the 9-o'clock position. It was decided again to attempt a surgical reattachment.

When the operative site was exposed a dark mass was noted bulging through the sclera (arrow in fig. 12). The eye did not transilluminate directly or indirectly through this area. Because of the history and these findings the mass was thought to be a malig-

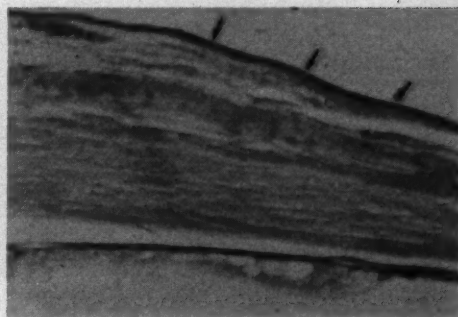


Fig. 15 (Tamler). Arrows point to epithelium which has grown posteriorly over the superior surface of the globe beyond the ora serrata.

nant melanoma. The eye was enucleated.

Histologically the mass turned out to be a scleral cyst (fig. 13). On higher power (fig. 14) the cyst was lined by stratified squamous epithelium and contained remnants of fibrin, degenerating red blood cells, inflammatory cells, and granular debris. The dark appearance of the cyst on the operating table was probably due to the old blood it contained.

Another patient had two diathermy operations for retinal detachment, one in April, 1949, the other in September, 1949. In 1951, a cataract was removed from the same eye.

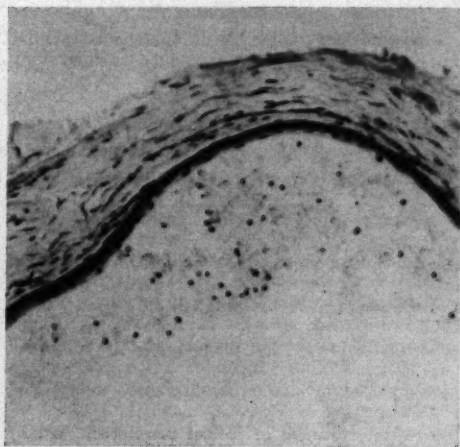


Fig. 14 (Tamler). High-power view of cyst shown in Figures 12 and 13.

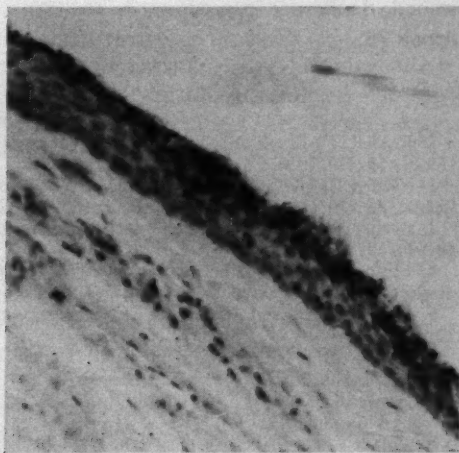


Fig. 16 (Tamler). Appearance of epithelium at high power.



Fig. 17 (Tamler). Epithelial-lined cyst was present in the outer layers of the sclera.

Subsequently the eye became blind and, in 1954, it was removed. Grossly the eyeball manifested considerable diathermy scarring on its superior surface. On sectioning the globe, it was noted that the retina was totally detached and the choroid was peppered with diathermy scars. Histologically it was seen that epithelium (arrows, fig. 15) had grown posteriorly over the superior surface of the globe beyond the ora serrata. Figure 16 shows the appearance of this epithelium under high power. Anterior to the ora serrata an epithelial-lined cyst was present in the outer layers of the sclera (fig. 17). The presence of epithelium so far back on the surface of the globe is difficult to explain. Perhaps it developed after the first operation and then possibly the cyst was caused by implantation occurring during the second diathermy procedure in the same region.

Although the cysts occurring in the last

two cases cannot be definitely ascribed to the diathermy procedures, the sequence of events in each case suggests a cause and effect relationship.

SUMMARY

The effect of diathermy employed in retinal reattachment operations on the coats of the human eye at different intervals of time following operation is illustrated by pathologic specimens.

A suggestion for avoiding damage to vortex veins is made.

Two cases receiving intensive diathermy and containing epithelial-lined scleral cysts in the region of the diathermy are presented to show a possible complication of diathermy procedures.

Clay and Webster Streets (15).

ACKNOWLEDGMENT

I am indebted to Dr. A. E. Maumenee and Dr. D. K. Pischel for their assistance in this study.

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SPECIES DIFFERENCES IN THE RADIOSENSITIVITY OF THE LENS*

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Effects of ionizing radiations on the lens have been studied extensively in rabbits and mice. In other species, such as dogs,¹ cats, simians^{2,3} and humans,^{4,5} reliable data on radiation effects on the lens are either not available or scarce. Moreover, even observations reported by different investigators on the rabbit and mouse lens are at variance with regard to cataractogenic threshold doses. Breed and age of the experimental animals and differences of the irradiation techniques and biomicroscopic methods can account for a good part of the inconsistencies of results when the same dose of a specific ionizing radiation was used. The described high tolerance of dog and monkey lens, however, convey the impression that a species factor is implicated in the radiosusceptibility of lens tissue.

Comparative biomicroscopic, histologic, and cytologic studies of irradiated lenses of laboratory animals have not been published in the past except for systematic investigations on early stages of radiation damage in the rabbit lens^{6,7} and a recent report by Kandori on rabbits, rats, and monkeys,^{8,9} in which the number of experiments is not mentioned.

It is the purpose of the present work possibly to narrow, on a morphologic level, gaps in the knowledge of the pathogenesis of radiation cataract by such a comparison. Bio-

microscopic observations were extended to four months, and in some instances to one year, and related to cytologic and histologic changes in the lens epithelium and lens fibers to obtain information, first, on the sequence of radiation induced lens changes and, second, on the relative radiosensitivity of the various tissue components in different species. Mice, rats, guinea pigs, rabbits, cats, dogs, and monkeys of both sexes served as experimental animals in this study.

METHODS AND MATERIALS

The right eye of each animal was exposed to 1,000 r X rays from a 210 kv. source through 0.5 mm. Cu. and 1.0 mm. Al.; other radiation factors were: 20 ma.; 145 r per minute; 30 cm. target lens distance; half-value layer, 1.0 mm. Cu. Round apertures in lead absorbers limited the beam to diameters of five, eight, 10, or 20 mm., depending on the size of the eye in the individual species. The animals were kept under light sodium pentobarbital anesthesia during irradiation. The left eye remained outside the beam and was protected against stray radiation as well as possible. The age of the animals could not be determined with accuracy, but albino rats of the Sherman strain and mice of the Swiss strain* were 10 to 12 weeks old; guinea pigs about three months; and rabbits about four months. Dogs, cats, and Rhesus monkeys were estimated to be from one to two years old. With the exception of the simians, the animals were considered sexually mature adults.

Previously described techniques⁸ were used for routine biomicroscopic examination, cytologic studies on whole mounts of the epithelium of lenses by means of the

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* Inbred in the Radiological Research Laboratory of Columbia University.

Feulgen reaction, and histologic examination of paraffin or celloidin sections of such lenses.

Incidence of cell division in the irradiated lens was expressed in percentage of normal control eyes and as absolute values. The number of degenerate cells was recorded per total population and also calculated per 100,000 cells to collate the results obtained from eyes of different size. It was necessary, therefore, to estimate the number of cells in the lens epithelium of normal animals in each species. A previously outlined technique was employed for this purpose.⁸

As a rule, observations covered periods of from two days to 16 weeks after irradiation. In rats, rabbits, and guinea pigs they were extended to one year or 14 months. Because of the frequent occurrence of congenital lens opacities, particularly in mice and rats, all eyes were examined with the Goldmann slitlamp prior to irradiation.

About 600 eyes were used for biomicroscopic, cytologic, and histologic examination, exclusive of another 600 preparations on which the average figures on mitotic activity of the rat and rabbit lens were based. This great number of preparations was required because of the many intervals at which the animals were killed and in view of random variations in the radiosensitivity of biologic material, even if such material is of homogeneous nature. Individual subgroups, however, consisted of from three to nine animals (in the monkey series only one to two because of incidental death) and precluded statistical evaluation. The high death rate of Rhesus monkeys in our series also made it impossible to study, in sufficient number, later stages of radiation effects on the lens.

EXPERIMENTAL RESULTS AND COMMENTS

BIOMICROSCOPIC OBSERVATIONS

In the focused beam of the Goldmann slitlamp radiation-induced lesions of the lens became visible earliest in guinea pigs: nine

out of 11 showed changes about two months after exposure of the eye to 1,000 r. The respective figures for mice were three months (19 out of 21 animals) and four to five months for rabbits (12 out of 12 animals) and rats (nine out of 14 animals). Initial changes appeared in cats (12 animals) after two, three, or four months and in one instance even after one month. In this group the unknown age of the animals may have affected the varying latency periods. Only one out of 12 dogs exhibited minimal lens changes four months after exposure to the X-ray beam, despite extensive epilation and severe inflammatory reaction of the lidskin at an earlier period. Rhesus monkeys did not develop lens opacities during an observation period of four months. In the series of the last three species the experiments were terminated at the four-month interval because of the high death rate in the colonies. If dogs and monkeys are excluded, the onset of initial biomicroscopically visible signs of radiation damage, then, differed to a moderate degree only in the species under study.

The early lens changes which followed the local exposure to 1,000 r X rays displayed striking morphologic similarities in all species. They appeared mostly as white or grayish small specks or elongated opacities and only occasionally as fine vacuoles. The round or streaky dots were scattered in the posterior cortex and/or, in smaller number, in the anterior cortical layers. Vacuoles were located near the anterior capsule.

The lesions increased in number with time, conflated to larger plaques, and, in the rabbit lens, progressed to the formation of densely packed granular opacities along the horizontal posterior suture. This predilection of a suture system for aggregation of small opacities was not observed in the other species.

At time-intervals from four to 12 months after irradiation, diffuse silky opacities developed in various sectors of the posterior lens cortex in mice, rats, guinea pigs, and

TABLE 1
AVERAGE NUMBER OF CELLS IN THE LENS EPITHELIUM OF VARIOUS MATURE ANIMALS

| Species | Mice | Rats | Rabbits | Cats | Dogs | Monkeys |
|----------------------------|--------|--------|---------|------------|------------|------------|
| No. Eyes Used for Average | 7 | 9 | 9 | 3 | 4 | 4 |
| Age in Months | 2 | 2-3 | 4-16 | 12 or more | 12 or more | 18 or more |
| No. of Cells | 40,661 | 99,781 | 741,205 | 1,061,450 | 1,141,300 | 343,452 |
| Average Life Span in Years | 2-3 | 3 | 5-7 | 9-10 | 10-12 | 12-14 |

Two eyes of humans, age 50-60, were prepared and the epithelial cells estimated.
The average figure was 732,048.

rabbits. Later the anterior cortex underwent similar changes. Such advanced lesions were not seen in cats and dogs during the 16-month observation period. The control lenses did not show opacities except those congenital cataractous changes which were observed before exposure of the right eye to the radiation source.

In contrast to effects of higher doses of X rays, vacuole formation was not a prominent feature of early lens changes. When they formed at later stages they were of small size and number and mostly seen anteriorly under the lens capsule. Guinea pig, cat, and dog lenses appeared free of vacuoles.

STUDIES OF WHOLE MOUNTS OF LENS EPITHELIUM WITH THE FEULGEN REACTION

Normal lens epithelium. Estimates of the normal cell population obtained from several epithelial preparations of each species are contained in Table 1. Counts on young adult guinea pigs were unobtainable because of

the difficulties in satisfactorily separating the epithelium and capsule from the cortex. The span of differences between species cell counts is signified by the mean value in mice (about 41,000) and that in dogs (about 1,100,000). Cell counts of Rhesus monkeys (343,000) averaged half those of rabbits. Preparations of two normal human eyes (age 50 to 60 years) were examined for comparison; their cell population of about 730,000 approximated the figures procured from rabbits. Table 1 also lists the average longevity of the studied species.

The mitotic activity of the normal lens epithelium—shown in Table 2—was determined for adults, and (in rabbits, cats and dogs) also for animals a few weeks old. Among the adult animals the number of dividing cells from rabbit lenses (175 mitoses) exceeded by factors varying from two to 17 the respective figures of other species when the comparison was based on counts of the whole mounts. Monkey lenses ranked last in the list with only 10 dividing cells

TABLE 2
AVERAGE NUMBER OF DIVIDING CELLS IN THE LENS EPITHELIUM OF NORMAL ANIMALS OF DIFFERENT AGES

| Species | Mice | Rats | Rabbits | | Cats | | Dogs | | Monkeys | Guinea Pigs | | | |
|------------------------------------|-------|-------|---------|------------|---------|-------|------------|---------|---------|-------------|---------|-------|-------|
| Age | Adult | Adult | Adult | 2-4 wk old | | Adult | 1-2 wk old | | Adult | 2-3 wk old | | Adult | Adult |
| No. Eyes Used for Average | 32 | 67 | 515 | 7 | | 18 | 5 | | 24 | 10 | | 13 | 4 |
| No. Dividing Cells per preparation | 42 | 70 | 175 | 414 | deg. c. | 72.6 | 191.4 | deg. c. | 43.5 | 220 | deg. c. | 10 | 34 |
| | | | | | 0 | | | 184.4 | | | 40 | | |
| Per 100,000 Cells | 101 | 70 | 24 | 0 | | 7.3 | | | 4.4 | | | 2.9 | |

deg. c.: Number of degenerate cells per preparation.

per preparation. These proportions changed in part when the number of mitoses were calculated per 100,000 cells. Mice and rats, then, were the species with the greatest mitotic activity (101 and 70 respectively) and dogs and monkeys those with the lowest (4.4 and 2.9 respectively).

The number of dividing cells per total population of lenses in very young rabbits, cats, and dogs surpassed those in adults from 2.4 to five times. The epithelium of kittens and puppies contained a considerable number of cells with signs of nuclear fragmentation; this phenomenon was not observed in rabbits, nor in lenses of adult animals except for a few of such cells per preparation.

Radiation effect on mitosis. The irradiation of one eye with 1,000 r X rays resulted in suppression of mitotic activity in all species, but the inhibition varied in extent and in length of time. The first counts were obtained, as a rule, 48 hours after irradiation to avoid anesthesia-induced changes, though the sodium pentobarbital anesthesia was light and brief. Most experiments were terminated two, four, seven, 14, 21, 28, 56, 84, and 112 days from the day of exposure. Cytologic studies on rabbits and rats were also carried out one year after irradiation, and 12 guinea pigs were killed at a 14-month interval, with a few preparations obtained at the eight-week period. The epithelium of this species could be peeled off the cortex successfully at later stages.

Mice and, to a less degree, rats displayed such rapid recovery from the initial depression of mitosis at the 48-hour interval that epithelial preparations of mice were also evaluated one day after exposure; moreover, attempts similar to those reported on in previous experiments on rabbits were made to study the effect of 1,000 r X rays on the mouse and rat lens within the first hour after exposure. In contrast to observations on the rabbit, phase counts on mice carried out after 10, 20, and 30 minutes did not demonstrate the characteristic disappearance rates of prophases, metaphases, and telo-

phases in regular sequence; at the 40- and 50-minute interval, however, prophase counts were much lower than the figures for metaphases and telophases.

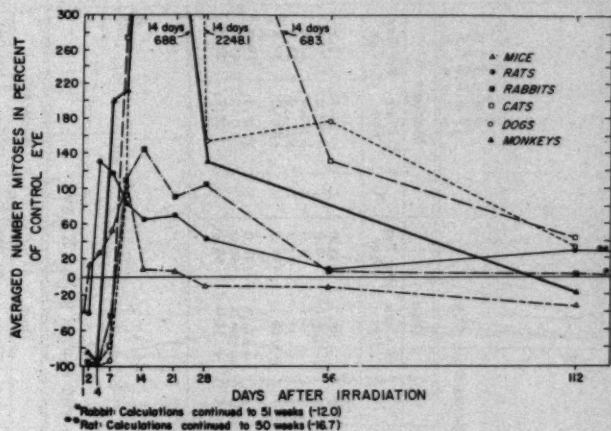
The over-all inhibition did not exceed 70 percent of the mitotic activity of the control eye and climbed to about 40 percent at the 24-hour interval. Similar responses were observed in rats, but the disappearance of the various phases of cell division followed in more orderly succession. Maximal depression amounted to 70 percent of mitotic activity of the control eye 50 minutes after irradiation and reached 40 percent of the counts in the control eye at the 48-hour interval, at a time when the epithelial preparation of mice already exhibited an overcompensating increase of cell division of 24 percent.

In other species the depression of mitosis was complete or almost complete and lasted longer. Figure 1 illustrates the absence of dividing cells in the preparation of rabbits, cats, and dogs for four days. In monkeys an occasional mitotic figure was seen during this period. In cats, dogs, and monkeys partial inhibition, slightly above the zero level, continued for seven days. After four and seven days, respectively, recovery was extremely rapid in dogs, monkeys, and cats and somewhat lower in rabbits. The overcompensating increase of cell division which followed recovery reached the highest peak level in dogs with 2,248 percent.* For cats the peak level was 682 percent and for monkeys it was 687 percent.

The relative values illustrated in Figure 1 are collated with the absolute numbers of mitoses in irradiated lenses in Table 3, which also lists the number of averaged experiments. Thus, the increase of dividing

* The number of mitoses in the normal epithelium of dogs fluctuates from animal to animal in a wider range than in other species. The ratio of counts of the experimental to the normal eye may well be exaggerated by this fact. The average difference in mitosis between right and left eye was sometimes greater in other species than in rabbits (less than 10-percent).*

Fig. 1 (von Sallmann, et al.). Effect of 1,000 r X rays on the mitotic rate of the lens epithelium of mice, rats, rabbits, cats, dogs, and monkeys.



cells to 687 percent of the control eye in monkeys corresponds to a figure of only 37 mitoses in the preparation, whereas the rate of 682 percent in cats corresponds to 534 mitoses in the cat lens epithelium.

The periods during which the number of dividing cells in the experimental eyes exceeded that in the control eyes varied with the species. In mice control levels were reached in about four weeks and were succeeded by a slight decrease during the following 12 weeks. In rats and rabbits the counts of the irradiated eye approached the counts in the control eye after eight weeks; in cats, dogs, and monkeys the decline was slower and lasted about 16 weeks. From this time on a moderate excess of dividing cells still persisted in the preparations of the irradiated eyes of cats, dogs, and, at this period, of rats. The counts obtained from rats and rabbits about one year after irradiation were just slightly less than those in the control eyes.

The effect of 1,000 r X rays on the mitotic activity of the lens epithelium, therefore, changes with the species. The inhibition is shorter and partial in mice and rats and almost complete and longest in cats and dogs. The most impressive difference between the various species is the extent and duration of the subsequent overcompensating increase of cell division in dogs and cats. The rela-

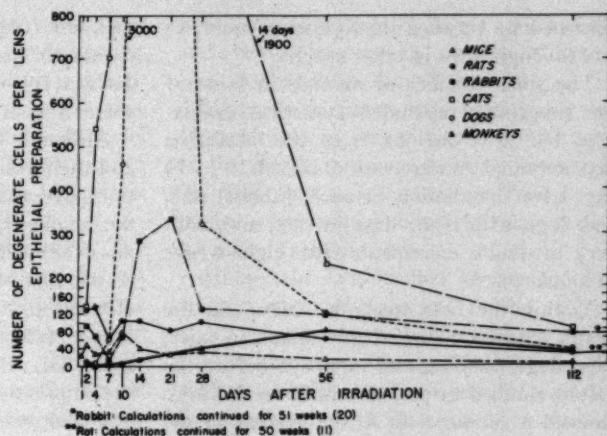
tive and absolute numbers of dividing cells in the experimental eyes of those species surpassed by far those observed in other groups.

Cell degeneration as radiation effect.

Clumping of chromatin, extrusion of Feulgen positive material from the cell nucleus, and the emergence of pathologic mitoses have been described in previous papers as early radiation effects in the rabbit lens. The epithelial preparations of normal adult or very young rabbits as a rule contain not more than a small number (one to eight) of degenerate cells per population. In this respect young cats and dogs differ greatly from rabbits. The lens epithelium of kittens and puppies from four days to two weeks old showed many cells with signs of nuclear fragmentation. An average of 1,840 degenerate cells per preparation was counted in kittens and 400 such cells or cell residues were averaged in puppies (table 2). The lens epithelial preparations of adult animals, however, were either free of such changes or the small number of degenerate cells did not exceed that noted in other species. Examination of the lens epithelial layer could not be extended to very young rats and mice because of technical difficulties in obtaining complete mounts of the epithelium from such small eyes.

Similar to observations in the rabbit lens

Fig. 2 (von Sallmann, et al.). Average counts of degenerate cells in whole lens epithelium after irradiation with 1,000 r X rays.



radiation-induced fragmentation of cell nuclei and extrusion of chromatin material are the preponderant morphologic phenomena of pathology in early stages of the X-ray damage in other laboratory animals. These radiation effects are shown graphically per whole population in Figure 2 and are calculated per 100,000 cells in Figure 3. Table 3 lists both series of values and the number of experiments in the 122 individual subgroups.

During the period of partial or complete inhibition of mitosis in the various species, the incidence of the change was low in dogs and monkeys. When calculated per 100,000 cells the injury was most extensive in mice and rats during the first two postirradiation

days. As described before, the depression of cell division in these groups was partial and short-lasting, but in the following days and weeks the impression of widespread X-ray induced injury to the epithelium of rats and mice was substantiated.

The number of damaged cells in the epithelium of dogs (300 per 100,000 cells) and cats (190 per 100,000 cells), however, far surpassed or reached the maximal figures established for mice (190 per 100,000) and rats (100 per 100,000). This radiation effect on the lens epithelium of monkeys remained of low order throughout the 16-week period after exposure to the X-ray beam. The incidence values of the change in rabbits were

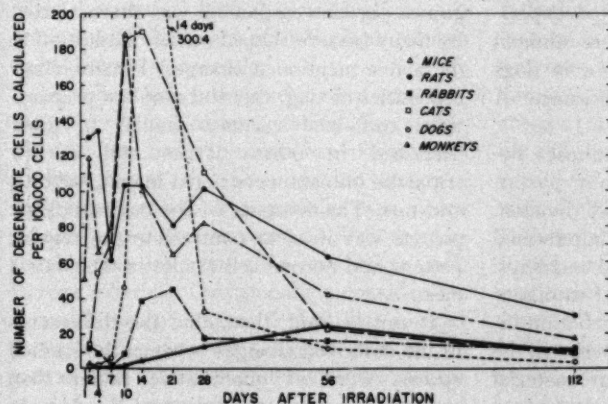


Fig. 3 (von Sallmann, et al.). Average counts of degenerate cells in lens epithelium after irradiation with 1,000 r X rays calculated for 100,000 cells.

intermediate between the figures in monkeys and the high rates in other species.

The small number of animals in some of the subgroups precluded statistical evaluation, but it is obvious from the tabulation that maximal counts were obtained 10 to 14 days after irradiation in mice, rabbits, cats, and dogs, after four days in rats, and, with very moderate increment, after eight weeks in monkeys.

Within the first week the curves in the graph showed a dip of the counts in mice, rats, dogs, rabbits, and monkeys before the values climbed to peak levels. Rats and mice showed a similar dent in the descent of the curves. At the 16-week interval the number of damaged cells was reduced to about one tenth of the maximal counts in mice, cats, and dogs and to about one third to about one fifth in rats, rabbits, and monkeys. The described signs of radiation-induced cell damage were still present in lenses of rats and rabbits about 12 months after exposure of the eyes to 1,000 r X rays, but the incidence of the lesion was low (11 and 2.7 per 100,000 cells, respectively). The results of the examination of the guinea pig lens epithelium were not tabulated because data were available only in the later stages. Few degenerate cells were seen at the two- and 14-month intervals.

Thus, quantitation of radiation induced signs of nuclear damage showed great differences among the studied species of experimental animals. These changes were minimal in Rhesus monkeys and excessive in dogs and cats. The questionable significance of the lesion will be discussed later.

Various forms of pathologic mitoses became visible during the period of postinhibitory recovery and excessive cell division. They were noticed in all species but seemed less numerous in dogs, cats, and monkeys. In previous work it was proposed to distinguish between two types of radiation-induced extrusion of chromatin material in the lens epithelium: clumped nuclear material of round contour often arranged in clusters,

and, less frequently, angular, sharp-cornered chromatin particles which are most likely derived from the disintegration of chromosomes at later phases of cell division.

Although both types of degenerate cells and their residues were observed in preparations from all studied species (except for the monkey), the globular type prevailed to an overwhelming degree in dogs and cats at the time when the degenerate cell counts climbed to the reported high peak levels. These forms, being interspersed between epithelial cells of normal shape, conveyed the impression that here extrusion of Feulgen positive material did not cause cell death or severe cell damage; the normal pattern of the epithelium was not interrupted by gaps due to vanished or vanishing cell elements.

Later stages of the radiation injury to the epithelium exhibited the usual cytopathology: accessory or micro nuclei were seen in all laboratory animals and often in great number. Marked differences in the size and staining intensity of the nuclei was another common finding. Giant nuclei, multinucleated cells, and vacuolar cell degeneration were recorded in the examination of cat, rabbit, and guinea pig preparations. Considerable irregularity in the arrangement of cells and paucity of cell elements in the pre-equatorial and equatorial zone predominated in the preparations from mouse, rat, and rabbit lenses. Fourteen months after irradiation the guinea pig lens epithelium was characterized by many bizarre-shaped nuclei in addition to the above mentioned changes. Finally, some cell nuclei of dog, cat, and monkey preparations contained vacuoles similar to those described in other tissues and a few tripartite mitoses were noted in cats, rabbits, and rats. The diversity of the cytopathologic picture was in clear contrast to the regular pattern and normal cell shapes in the control eyes.

It can be said, then, that the differences in the described changes between the studied species were of quantitative rather than qualitative nature: the extent of the damage

was greater in the mouse, rat, rabbit, and guinea pig than in the other three species. Although the incidence of nuclear fragmentation greatly diminished within months, other signs of radiation injury to cell nuclei were extensive one year after irradiation in the three species examined at this long interval.

Lens fiber changes as radiation effect. The evaluation of fiber and cell changes in sections of celloidin or paraffin-imbedded lenses met with the well-known difficulties of histologic studies on such material. Breaks in the sections and distortion of preparations by irregular stretching during the mounting precluded assessing the radiation effects on a quantitative basis, as was attempted in previous work on the rabbit lens.⁸

In these studies the number of nuclei in the lens bow which indicated positional changes and the number of epithelial cells in a measured part of the bow near the equator were compared with the corresponding nuclei and cells of the individual control eye. This procedure could not be followed in the present study because of the small number of imbedded lenses of the different species at given intervals. Attention centered on changes of the nuclei of the lens bow and migration of cell elements from the posterior margin of the germinative layer and in later periods on the displacement of cells into various layers of the cortex and signs of fiber destruction. The nonirradiated, identically processed lenses of individual animals served again as controls.

In mouse lenses the nuclei were seen frequently within hydropic cortical fibers; this phenomenon and the migration of cells into various layers of the posterior cortex—partly underneath the capsule—was much more marked than in cats and dogs at comparable time intervals after irradiation (two to four months). Occasionally a considerable accumulation of migrated cells was noticed in the cortex near the posterior pole of the mouse lens. Also in this species, poorly stained and fragmented nuclei were scattered

over wide areas in later stages (six months) and were observed in swollen, distorted, and irregularly arranged lens fibers.

Hydrops of fibers was particularly well demonstrable in the anterior cortical layers of the guinea pig lens in cross sections of the fibers but was not accompanied by extensive migration of cells or displacement of cell nuclei from the bow.

Among the five studied species the fiber changes were least marked in the cat; positional changes in the bow nuclei were minimal. In the clinically clear lens of the dog swollen lens fibers were visible in considerable number behind the equator in the bow area (six or eight weeks after), whereas the migration of cells or cell nuclei within the fibers was inconspicuous.

The comparison of the radiation effects in the different species indicated that fiber changes did not always parallel signs of nuclear degeneration and cell migration from the equator into the various layers of the cortex. However, nuclear debris was often imbedded in proteolyzed fibers.

COMMENT

The analysis of data obtained from mitotic and degenerate cell counts in whole mounts of the lens epithelium in six of the seven examined species (early stages of postirradiation changes in guinea pigs were not available) revealed striking differences of radiation effects in some respects and similarities in others: it has been shown in a previous study¹⁰ on the radiobiologic effectiveness of radiations of different linear energy transfer that the induced depression of cell division and subsequent excessive rise of this function is but loosely associated with the cataractogenic properties of these radiations, that is, a relationship can be construed only to the extent that degree and continuance of inhibition are dependent on dose, within limits.

The short-lasting and partial impediment of cell division paired with the relatively rapid development of cataractous changes

in rats and mice and—on the other hand—the prolonged and almost complete depression in dogs and monkeys which did not exhibit lens opacities 16 weeks after the exposure to the same dose of X rays (1,000 r) also pointed to a dissociation of the two radiobiologic events. However, basically inhibition and overshooting of cell division in the lens epithelium followed the irradiation of the eyes in all species.

In earlier work¹⁰ the incidence of radiation-induced nuclear fragmentation in the total cell population one or two weeks after exposure was taken as a reliable indicator of the severity of the injury to the lens; in fact it was thought possible to predict at this early state—solely on the basis of the number of injured cells in the rabbit lens epithelium—whether or not a given dose of ionizing radiation would produce cataractous changes.¹¹ In mice and rats the great number of degenerate cells (per 100,000) appeared also causally related to early onset and progress of lenticular opacities. Such an interdependence was not observed in cats and dogs.

It has been reported in the results that the lens epithelium preparations of normal very young puppies and kittens contain a great number of extruded chromatin globules in contrast to young rabbits and to adult animals in general. Irradiation of adult cats and dogs with 1,000 r X rays induced, at the period of overshooting cell division, a burst of free, round chromatin particles without widespread destruction of cell nuclei. In these instances the appearance of chromatin fragments between normally shaped and arranged cells in all zones of the surface epithelium could not be incriminated as attesting the destruction of cell elements and early development of lenticular opacities.

A distinction must be made, then, between the extrusion of Feulgen positive material from the cell nucleus as an expression of the effort of the cell to preserve its nucleus cytoplasm relationship and the lethal loss of chromatin from the nucleus. The latter type of cell degeneration, leading to cell death, prevailed in mice, rats, rabbits, and

possibly guinea pigs, whereas the widespread scattering of chromatin globules in the central zone as well as in the periphery of the epithelium of dogs and cats has little pathognomonic significance. The lesions in monkeys were numerically of a low order and thus do not contribute to the point under discussion.

It is held by the majority of investigators that ionizing radiations first injure the lens epithelium, predominantly its germinative zone, by a still controversial radiobiologic mechanism. The fiber changes of later stages which represent the main substrate of lens opacities are supposed to result directly or indirectly from this damage to the epithelium. This concept is supported by the differences in onset between the signs of nuclear fragmentation and fiber lesions and by the migration of nucleated elements into cortical fiber layers before major lens opacities become visible. In the present study the observations on mice, rats, and rabbits constitute further evidence for the correctness of this theory, but in guinea pigs and dogs, hydrops of fibers was noted independent of marked proliferation of nucleated elements within four months after radiation. Monkey lenses were not sectioned in this study. It is unlikely at the present time that these dissimilarities in the sequence of pathologic events are connected with fundamental variations of the X-ray effect on the lens in the studied species.

The delay in development of cataractous changes in dogs and monkeys under the conditions of the experiment suggests greater tolerance of the lens of this species to ionizing radiation, but the microscopically visible lesions of cells of the surface epithelium and of the fibers in dogs four months after irradiation do not substantiate the impression of an extraordinary resistance of the lens in this species to the radiation.

Lenses of adult monkeys and dogs have the smallest number of dividing cells (calculated per 100,000 cells) among the studied animals. The low mitotic rate in their germinative zone may be connected with the

relative radiosensitivity of such lenses, since Cogan and Donaldson⁷ have reported on the decrease of the lens vulnerability with increase of age. The great number of dividing cells in very young rabbits, cats, and dogs thus might parallel the high radiosensitivity in these age groups. The lens epithelium preparation obtained from one puppy 10 days after irradiation of the eye with 1,000 r X rays was covered with chromatin particles which apparently originated from the degeneration of dividing cells (1,409 instances of chromatin extrusion in the preparation of the small lens).

The examination of flat preparations of the epithelium and of celloidin sections of the irradiated lens disclosed a depletion of cell elements, particularly in the germinative zone of this cell layer, in mice, rats, guinea pigs, and rabbits and a great variety of signs of cell degeneration such as accessory, micro, and giant nuclei, multinucleated and blister cells irregularly arranged, and stained nuclei of bizarre shapes. These changes were less pronounced in cat, dog, and monkey preparations.

Proliferation of cells or cell elements into various layers of the cortex was also more extensive in the aforementioned group of animals but was by no means absent in the second group.

The well-known processes of disintegration and degeneration of such cells and the equally well-known signs of hydrops and proteolytic decomposition of fibers also differed only quantitatively between the two groups of animals.

It can be concluded, then, that species differences of radiosensitivity of the lens to an isodose of X rays were real on a quantitative basis, but radiation-induced cell or fiber damage was qualitatively comparable in all examined laboratory animals.

SUMMARY

1. The effect on the lens of local irradiation of one eye with 1,000 r X rays was studied in mice, rats, guinea pigs, rabbits,

cats, dogs, and monkeys. Biomicroscopic, histologic, and cytologic examinations were carried out at 10 or 12 intervals, ranging from one day to 116 days, and in three species to one year after exposure. About 600 eyes were used in this part of the study.

2. The lens epithelium of normal eyes of adult animals contained dividing cells in ratios per 100,000 cells varying from 101 (mice) to 4.2 (dogs) and 2.9 (monkeys). The number of dividing cells in the epithelium of very young rabbits, cats, and dogs are multiples of those found in adults. Extrusion of chromatin is a common finding in the lens epithelium of normal kittens and puppies but was not observed in very young rabbits.

3. Exposure to the X-ray beam induced depression or complete inhibition of mitosis which was short lasting and partial in mice and rats and continued close to zero levels for about one week in dogs, cats, and monkeys. This phenomenon was followed in all species by an overcompensating increase of cell division. The increment reached the highest peaks in dogs and cats.

4. Radiation-induced cell degeneration with nuclear fragmentation was extensive in mice, rats, and rabbits but was surpassed strikingly by a burst of extruded chromatin globules in dogs and cats. The distribution of these particles between normal regularly arranged epithelial cells suggests restoration of a disturbed nucleus-cytoplasm relationship rather than a lethal injury to the nucleus.

5. The onset of biomicroscopically visible lens opacities was delayed in dogs and monkeys as compared to other species. This fact and the characteristics and magnitude of cell proliferation and fiber lesions indicate a quantitative difference between dogs and monkeys and other species in the damage produced to the lens by the same dose of X rays. However, the lens of all animals responded qualitatively in the same manner to the radiation injury.

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ANGIOSCOTOMETRY IN GLAUCOMA*

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Glaucoma is one of the most baffling problems in ophthalmology, as well as one of the most serious. The importance of glaucoma as a major cause of ocular disability and blindness has unquestionably been realized from the time of Hippocrates. The large number of papers appearing in the literature and the divergent views expressed therein confirm the unsolved problems of this condition and emphasize its intriguing and serious nature.

The diagnosis of glaucoma in its earliest stages has always been of great importance because later on permanent damage to the ocular tissues takes place. A well-developed case of chronic simple glaucoma presents classic signs of raised tension, dilated sluggish pupil, cupping of the disc, and field defects, while diagnosis of a case in its earliest stages is sometimes a problem of utmost difficulty.

The finding of a normal tension on one or more occasions is no criterion that glaucoma does not exist. Investigation of the diurnal variations and provocative tests may be of some help only when they are positive and, even then, their value lies in the evidence they bear in association with other factors. There is no sequence of signs or symptoms of early glaucoma. While the peripheral field changes are in progress, the patient may feel little distress. It is usually after the central field has also become affected that the patient comes to the hospital. Rise of tension and cupping of the disc are late in onset.

Since the very beginning, field changes are considered to be among the early manifestations of the disease. Perimetry was first introduced to discover the more gross changes in the peripheral field. Scotometry on the Bjerrum's screen was later found to be a more delicate procedure, as it could discover an early scotoma in the central 25 degrees of the visual field. Recently the angioscotoma

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has been found to give a still more delicate and precise reflection of changes within the central 20 degrees of the visual field.

The angioscotoma was first described by Evans¹ as a "defect of the visual field coming from the blindspot of Mariotte and related in form to the pattern of distribution of the retinal vessel tree." These shadows after extensive research have been interpreted as arising through modifications in the functions of the retinal perivascular spaces² and in the retinal synaptic junctions.

The study of the angioscotoma in cases of glaucoma was first made by Evans³ in 1938. He correlated these changes with those in the fundus, vision, and tension, and concluded that angioscotometry illustrates more minute variations of the disease than are evident by any other single means. Since the angioscotoma is so sensitive to local and general pathologic conditions, and the changes in fundus, vision, and tension appear late, the correlation was not particularly clear. It was, therefore, thought that a comparison of the field changes on the perimeter and Bjerrum's screen with the changes in the angioscotoma might throw some light on early diagnosis of chronic simple glaucoma.

SELECTION OF CASES AND PROCEDURE

Two main criteria were kept in view while selecting cases; the patient should be intelligent enough to co-operate and he should have a very early case of glaucoma. As stated, diagnosis of early cases is extremely difficult.

For the present study those cases which manifested definite signs of glaucoma in one eye, while the other eye revealed no changes in the field, vision, tension, and the fundus, were chosen. For practical purposes, the second eye was considered absolutely normal. Another group of five patients who complained of vague early symptoms—so-called prodromal symptoms—of glaucoma was also used.

Twenty cases which showed no subjective or objective symptoms of glaucoma and were

of the same age group as is commonly encountered in the disease were used as controls. They were examined for vision, by perimetry, scotometry on the Bjerrum's screen, angioscotometry, funduscopy, and last of all for the tension.

A total of 21 glaucomatous patients were examined in the same way. Sixteen had one or more objective findings in one eye while the other eye was normal. The remaining five cases manifested a variety of symptoms, namely, appearance of colored haloes around bright lights, or stuffiness of the eyes, and so forth.

Before the eye examination, a thorough general physical examination was made in order to eliminate any general disease.

It was found best to keep the appointment during the early morning hours between 8:00 A.M. and 9:00 A.M. The patients were advised not to take any medication, either local or general, which influenced the intraocular pressure. Nervous excitement and physical exertion were avoided as far as possible. None of the patients were addicted to alcohol or tobacco.

Angioscotometry was done on an apparatus made according to the details given by Evans,⁴ with objects varying from 0.25 to 0.5 mm. in diameter.

OBSERVATIONS

The 20 control cases did not show changes in any of the investigations performed. Their blindspots measured about five degrees horizontally and seven degrees vertically. The angioscotomas were about two-degrees wide as they emerged from the blindspot, while peripherally they kept on tapering. They arched from the upper and lower poles of the blindspot and passed above and below the fixation point at a distance of about 10 degrees. These arches gave off branches peripherally which followed the dichotomous system of distribution. Out of 42 eyes of 21 glaucomatous patients, seven had absolute glaucoma and, therefore, could not be included in this study. The following observa-

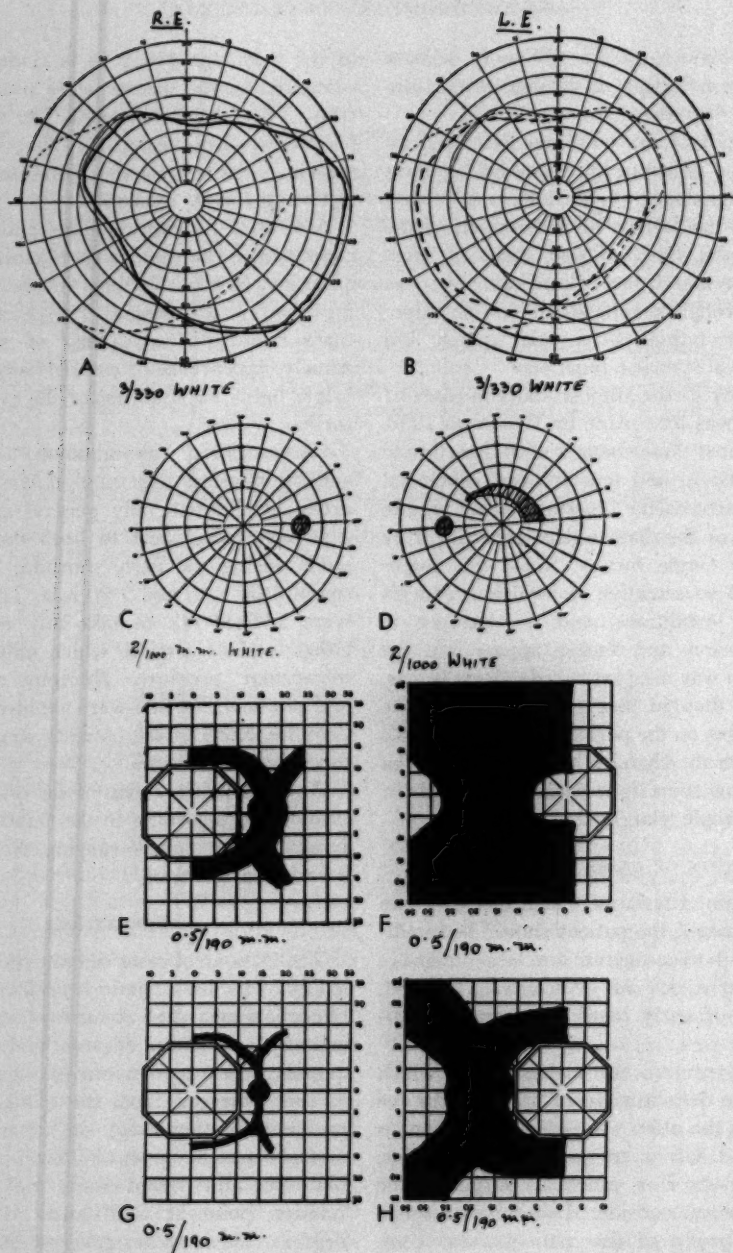


Fig. 1 (Mathur and Mathur). *A case report.* Patient S, a woman, aged 38 years, had a history of seeing colored haloes around bright lights. She suffered occasional attacks of mild pain in the left eye. Vision was: R.E. 6/6; L.E., 6/24. Tension was: R.E., 22 mm. Hg; L.E., 30 mm. Hg (Schiotz). The fundus of the right eye showed a deep physiologic cupping; the left eye was normal. Visual fields showed: (A and C) Right eye, normal. (B and D) Left eye, Rönne's step; Bjerrum's scotoma. Angioscotometry showed: (E) Right eye, ++. (F) Left eye, ++++. Angioscotometry after one-percent pilocarpine drops showed: (G) Right eye, normal. (H) Left eye, +++.

tions were made on the remaining 35 eyes:

The degree of widening of the angioscotoma has been represented in plus (+) and not in scotoma units.

(+) Out of the four scotomas charted the two arching above and below the fixation point showed widening.

(++) All the four scotomas were widened without a remarkable increase in the area of the blindspot.

(+++) When the blindspot was also widened but the temporal field not markedly affected.

(++++) When the temporal field was absent and the macular area was encroached upon.

Eleven eyes showed advanced angioscotometric changes, recorded as +++++; 15 showed fairly advanced changes (+++), five showed moderate changes (++), and four had slightly dilated angioscotoma (+).

It was interesting to correlate the angioscotometric findings with those of the intraocular pressure (table 1). Twenty eyes which had normal tension of below 25 mm. Hg (Schjötz), showed the following angioscotometric changes:

Five had widening of +++++, seven of +++++, four of ++, and four of +.

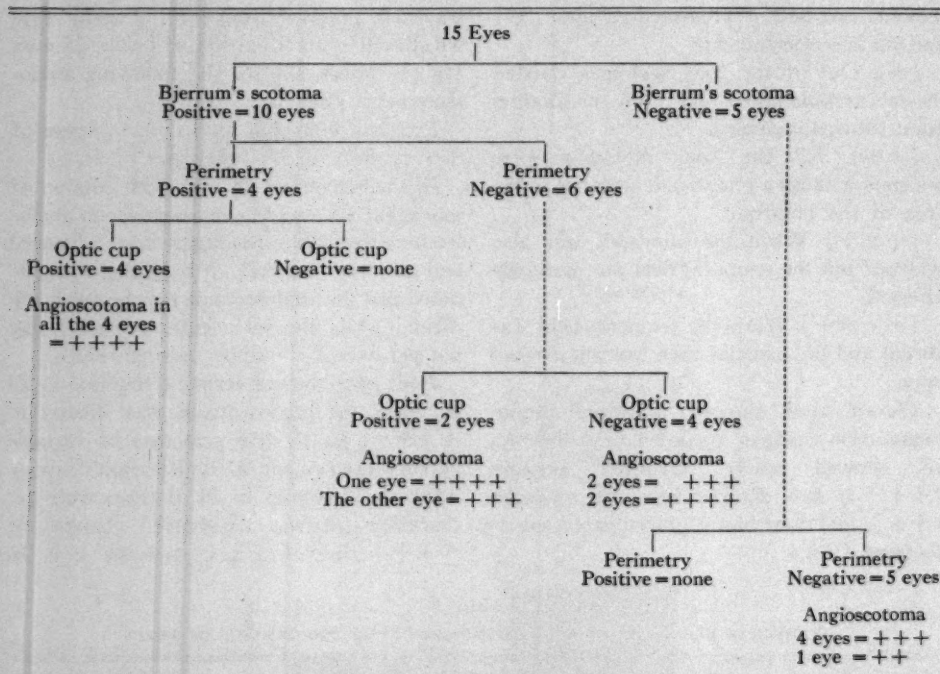
In the remaining 15 eyes with tension of more than 25 mm. Hg, the changes in angioscotoma were correspondingly more advanced and absolute (table 2). It may, therefore, be noted that the angioscotoma may be markedly dilated while the intraocular pressure may not yet exceed the upper normal limits.

Four eyes showed Rönne's step and in all of them the angioscotoma was dilated to +++++. In 18 eyes scotomas of variable extent were evident on the Bjerrum's screen. The angioscotomas in all of them were remarkably dilated: 12 showed changes of +++++, five of +++++, and one ++. In

TABLE 1
NUMBER OF EYES WITH INTRAOCULAR PRESSURE 25 MM. HG (SCHJÖTZ) OR BELOW

| 20 Eyes | | | |
|--|--|---|--|
| Bjerrum's scotoma Positive = 8 eyes | | Bjerrum's scotoma Negative = 12 eyes | |
| Perimetry Positive, none | | Perimetry Negative = 8 eyes | |
| | | Optic cup Positive, none | |
| | | Optic cup Negative = 8 eyes | |
| | | Angioscotoma | |
| | | 5 eyes = +++++ | |
| | | 2 eyes = ++++ | |
| | | 1 eye = ++ | |
| | | Perimetry Positive, none | |
| | | Perimetry Negative = 12 eyes | |
| | | Optic cup Positive, none | |
| | | Optic cup Negative = 12 eyes | |
| | | Angioscotoma | |
| | | 5 eyes = +++++ | |
| | | 3 eyes = +++ | |
| | | 4 eyes = + | |

TABLE 2
NUMBER OF EYES WITH INTRAOCULAR PRESSURE ABOVE 25 MM. HG (Schiøtz)



the remaining 17 eyes, no scotoma could be detected on the Bjerrum's screen, while the angioscotoma showed remarkable changes: nine showed a dilatation of + + +, four of + +, and four of +.

Eleven eyes had deep atrophic optic cupping, seven of which had absolute glaucoma and were eliminated from this study. Among the remaining four, two showed + + + +, and the other two + + + changes in the angioscotoma. In six eyes the optic cup did not extend up to the periphery of the disc but was rather deep. Angioscotoma of three of these showed + + + + dilatation, while the other three were dilated to + + +. Twenty-five eyes had normal optic discs. In five the angioscotoma was dilated to + + + +, in 11 to + + +, in four + +, and in four +. It may thus be noted that the optic cupping appears very late when angioscotomas have become extremely dilated.

In 12 eyes there were no field changes, acuity of vision and fundus were normal, and tension below 25 mm. Hg (Schiøtz). For all practical purposes they were considered as normal eyes. Five had angioscotoma dilated to + + +, three to + +, and four to +. In five other eyes, vision, field, and fundus were normal, the tension varied between 25 to 30 mm. Hg; in four the angioscotoma was + + +, and in one +.

Of the five patients with early symptoms of the disease who mostly complained of occasional heaviness in the head, all showed advanced changes in the angioscotoma. These cases were put on one-percent pilocarpine used as drops and the frequency was adjusted to the severity of the signs and symptoms. A regular check-up was made at suitable intervals. It was noted that the angioscotoma became reduced in size in every case, and in most of the cases up to + + + dilatation, it became more or less normal. With

the administration of pilocarpine, tension also went down, sometimes even to subnormal levels.

Under this treatment, the angioscotoma could be kept within the normal limits for months and none of the signs and symptoms progressed, except in two cases which developed subacute attacks and their angioscotomas dilated tremendously. These cases were later operated.

In three of the cases, on the first visit, a small scotoma, which could be detected on the Bjerrum's screen with a small green object, surprisingly disappeared with the use of pilocarpine.

DISCUSSION

At present great stress is being laid on the examination of field changes in early cases of chronic simple glaucoma, both for diagnosis and follow-up. With the introduction of the perimeter, grosser defects in the peripheral field could be investigated. Later, Bjerrum's screen demonstrated that early scotomas of glaucoma appeared in the central 25 degrees of the visual field. The present study shows that the changes in the angioscotoma appeared much earlier and were more delicate than those discovered by any of the previous methods. By the time a minute scotoma appeared on the Bjerrum's screen or the internal isopters became constricted, the angioscotometric changes were far more marked. Later, with the appearance of a more pronounced Bjerrum's scotoma and the rise of tension to the upper normal limits, the angioscotoma showed advanced changes. In some of these cases, fixation was difficult to maintain during angioscotometry. When tension was above normal, when the disc was pale and atrophic and the acuity of vision reduced, the case was beyond the scope of angioscotometry.

The patients with early glaucoma, who were suffering from the various prodromal symptoms, showed that a remarkable widening of the angioscotoma already existed.

Patients with glaucoma in one eye are said to have potential cases of glaucoma in the

other eye as well, although none of the symptoms or signs may be apparent. Such cases gave useful information in the present study for in all of them there was a marked dilatation of the angioscotoma. This further supported the view that changes in the angioscotoma were first to appear.

When early cases were kept on miotic treatment, the tension dropped to normal or even to subnormal levels. The angioscotoma regained its normal size in those cases in which no scotoma was detectable on the Bjerrum's screen, and even in those which showed a Bjerrum's scotoma, the reduction in the size of angioscotoma was remarkable. This seemed to show that widening of the angioscotoma was due to glaucoma and not to some other pathologic condition. This fact also helped in assessing the suitable treatment, for angioscotometry provided the most delicate method for follow-up.

Angioscotometry helps not only in the diagnosis but also in the prognosis and treatment of a case of glaucoma. The only disadvantages of this procedure are that it requires extreme co-operation of the patient, who should be intelligent, and that the disease should be of a very recent onset. Usually patients come to the hospital when the visual acuity of both eyes is affected and are, therefore, beyond the scope of angioscotometry.

CONCLUSIONS

The present study demonstrates the importance of angioscotometry in the diagnosis, prognosis, treatment, and follow-up of early cases of chronic simple glaucoma before changes can be demonstrated by other means.

The study further stresses that in those cases in which one eye is already affected with glaucoma, the other eye should be examined on an angioscotometer and a regular follow-up should be of great importance. As soon as the angioscotoma shows widening, suitable miotic therapy may be instituted. It may thus be possible to nip the disease in the bud.

Angioscotometry may also be useful in noting the effects of the various miotics, the

frequency of their use and the strength needed for a particular case.

SUMMARY

Twenty normal cases were examined by angioscotometry and used as controls for this study.

Thirty-five eyes of 21 glaucomatous patients were examined for angioscotometry, perimetry, visual acuity, fundus and tension changes.

In 20 eyes tension was below 25 mm. Hg (Schiotz); in all of them the angioscotoma was remarkably dilated. In the remaining 15 eyes with tension above 25 mm. Hg, the angioscotometric changes were correspondingly more advanced.

Four eyes, manifesting Rönne's step, had extremely dilated angioscotomas. Eighteen eyes had scotomas on the Bjerrum's screen; all had a remarkable widening of the angioscotoma.

Four eyes had deep optic cupping. The angioscotoma was extremely wide. Even those eyes with deep physiologic cupping showed marked changes in the angioscotoma.

Twelve eyes did not show any symptoms and were, for all practical purposes considered to be normal. In all of them the angioscotoma was notably dilated.

Five patients who had early symptoms of glaucoma manifested a remarkable widening in their angioscotomas. All these patients were put on one-percent pilocarpine drops. There was a marked reduction in the angioscotoma, with a corresponding fall in tension. By observing the angioscotoma the disease could be kept under control for months. Angioscotometry, therefore, not only helps in the diagnosis but also in prognosis, treatment, and follow-up of a case of chronic simple glaucoma.

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OPHTHALMIC MINIATURE

For these Semites, feeling themselves such shrews, have no confidence in man, but in God only; they would all see the leech's skill proved upon some other than themselves. Thus hardly do any come to the man of medicine till he be about to depart from them; when commonly only the most intractable or hopeless cases will be brought before him. Notwithstanding, they all love to babble-babble their infirmities, in the wholesome ears of the Hakim. As I have walked in Arabian villages, some have caught me by the mantle to enquire, "Eigh! thou the apothecary! canst thou not restore their sight to the blind?" So everywhere they brought me to help some whose eyes were perished.

G. M. Doughty, *Arabia Deserta*, 1921.

EXPERIMENTAL PRODUCTION OF FLASH BURNS IN THE RABBIT RETINA*

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Before the advent of the atomic bomb, the effects of thermal radiation on the eye had been studied extensively,¹ but only recently has the hazard of chorioretinal damage from nuclear explosions been recognized.² While only one case of retinal injury has been reported following the Hiroshima explosion,³ it was shown experimentally by Byrnes, and co-workers,⁴ in 1952, that such injury could be produced in rabbits exposed at distances of 42.5 miles from an atomic explosion, and in the past years, six cases of thermal injury to the retina as a result of atomic explosions have been reported.⁵ It, therefore, has become important to determine as accurately as possible the threshold dose necessary to produce irreversible burns of the retina. This study was undertaken in an effort to shed some light on the problem and this paper is a preliminary report of work still in progress under U. S. Air Force sponsorship.

The reason that retinal damage can be produced at distances far in excess of those at which flash burns are observed is because of the optical system of the eye. As one moves away from the fireball, the intensity of radiation at the cornea decreases as the square of the distance; at the same time, however, the area of the retinal image of the fire ball also decreases in the same proportion.

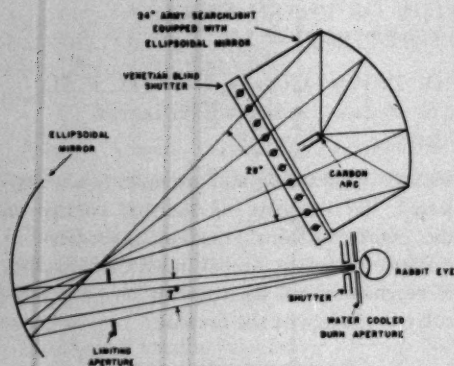
Hence, if scattering and attenuation are neglected, the intensity of thermal energy on the retina remains constant regardless of distance from the fireball until that distance is reached where the eye can no longer resolve the image of the fireball.

LABORATORY EQUIPMENT

Previous work in this laboratory had demonstrated the usefulness of a 24-inch Army searchlight equipped with an ellipsoidal reflector for the production of flash burns in animals and human volunteers.^{6,7} It was possible to produce thermal intensities of 22 to 23 cal./cm.²/sec. over a diameter of 0.5 inch, using standard 10-mm. high intensity carbons. However, this arrangement, while excellent for studies on flash burns to the skin, is not suitable for producing small retinal burns because the highly converging cone of radiation (28 degree solid angle) would produce a retinal burn covering a large part of the fundus. By employing a second ellipsoidal mirror to focus the real image from the first mirror we obtain a cone of radiation having a solid angle of seven degrees which more nearly simulates the atomic fireball viewed at an appreciable distance. For example, viewing the six-inch diameter cone of light reflected from the second mirror at a distance of 51 inches is equivalent to viewing a 900-foot diameter fireball at a distance of 1.45 miles.

On the assumption that the rabbit eye may be approximated by a lens of one cm. focal length, the retinal image of the fireball would have a diameter of about 1.2 mm. It must be emphasized, however, that the thermal dose delivered in one second by the fireball of a 20 KT weapon would be about seven to 10 times the thermal dose delivered by the laboratory source described here.

*From The Titmus Ophthalmological Research Laboratory and the Department of Biophysics, Medical College of Virginia. This research was supported by the U. S. Air Force under Contract No. AF-18(600)-1272, monitored by the USAF School of Aviation Medicine, Randolph Field, Texas. Presented before the American Ophthalmological Society, 92nd annual meeting, Hot Springs, Virginia, June, 1956. This paper will be published in the *Transactions of the American Ophthalmological Society* and is printed here with permission of the American Ophthalmological Society and Columbia University Press.

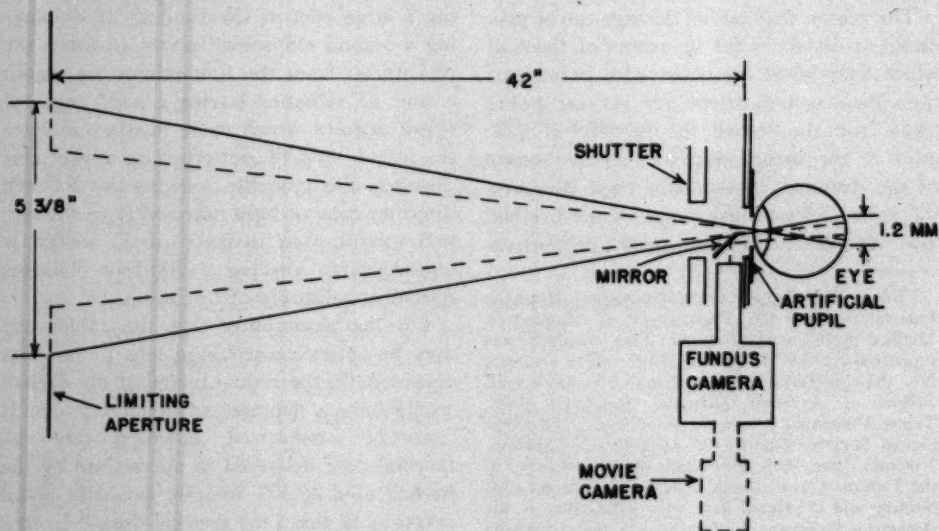
Fig. 1 (Ham, *et al.*). Apparatus used.

In this respect our simulation of the fireball is not realistic at distances where atmospheric attenuation can be neglected. However, as the distance from the fireball is increased to many miles, attenuation by absorption and scattering becomes appreciable in reducing radiation intensity. This attenuation is not present in the laboratory. Moreover, at great distances from the fireball, only those photons which have not undergone absorption or scattering will contribute to a well-defined image of the fire-

ball on the retina. Scattered photons will be distributed more or less uniformly over the entire retina.

To put it another way, the thermal intensity measured by an uncollimated black body receiver is greater than that intensity incident on the cornea which contributes to a retinal image of the fireball. Thus, as we proceed to great distances from the fireball the thermal intensity available for a definitive retinal image can be more closely approximated by a laboratory source, since the latter provides a constant thermal intensity on the retina regardless of image size.

A limiting diaphragm or aperture placed eight inches from the second reflecting mirror as shown in Figure 1 serves as a method for controlling the retinal image size. As the diameter of this aperture is reduced, the solid angle subtended by the rabbit eye becomes smaller, but at the expense of the thermal intensity incident on the cornea in direct proportion to the area of the radiation cone excluded. These two factors, solid angle and thermal intensity incident on the cornea, cancel out to maintain a constant thermal intensity on the retina (fig. 2). Under ex-

Fig. 2 (Ham, *et al.*). Apparatus used.

perimental conditions with a source of finite size and where the shadow of the carbon arc mount is focussed on the retina, there are practical limitations to the size of burns which can be produced.

Visual alignment of the rabbit is accomplished with a Bausch and Lomb fundus camera and a tiny mirror placed in the beam entering the eye. A 16-mm. movie camera can be substituted for the eyepiece, allowing photography of lesion production. Exposure time is controlled by a Compur shutter and is measured by means of a photomultiplier, an electronic gating circuit, a 10 KC oscillator, and a scaler. The photomultiplier tube operates the gating circuit which allows 10 KC pulses to feed into the scaler. The scaler indicates exposure time directly to 0.1 milliseconds.

In the retinal burn studies, National Carbon Company, 10-mm. diameter, Hitex positive carbons and Orotip negative carbons operated at 140 amp. D.C. have been utilized. Figure 3 illustrates the spectral distribution obtained with a Bausch and Lomb grating spectrometer and an Eppley thermopile. A 5,800-degree black body curve is shown for comparison. The carbon arc distribution is deficient in near infrared as compared to the black body at 5,800 degrees K.

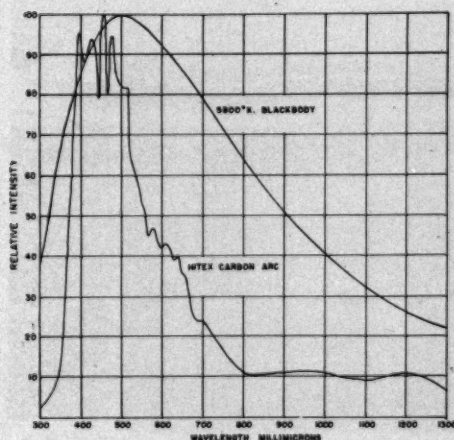


Fig. 3 (Ham, et al.). Spectral distribution.

Thermal intensity has been measured with a water flow calorimeter. The intensities available at the burn aperture range from 1.2 to 1.4 cal./cm.²/sec. Insertion of the mirror used with the fundus camera reduced this intensity about 10 percent. A venetian blind type of shutter mounted on the searchlight housing provides a means of reducing intensity to any desired level (fig. 1).

EXPERIMENTAL PRODUCTION OF RETINAL BURNS

Mature Chinchilla gray and New Zealand black rabbits, weighing from 3,000 to 5,000 gm., were used in these studies. Refractive error and corneal curvature were measured in all animals used in order to assure ocular uniformity. The geometric axis also was measured in a number of enucleated eyes. Animals with too much variation in pigmentation of the fundus were eliminated from the study. Sodium nembutal (25 mg./kg. body weight) was used for intravenous anesthesia; the pupils of all animals were dilated with atropine prior to exposure and the nictitating membrane excised.

The animal to be exposed was then rested on an adjustable platform and the eye held against a plastic annulus inserted in the burn aperture; an aperture, eight mm. in diameter, was used to define the pupillary diameter. The animal's dilation was greater than eight mm. in all cases. The fundus was then viewed through the fundus camera with the Venetian blind shutter almost closed. When the radiation was on a desired spot, the exposure was given by the operator of the fundus camera. At the same time a motion picture of the exposure at approximately 70 frames/sec. was taken.

Exposures of 500 to 1,000 m. sec. immediately produced round or slightly oval lesions of a dense white appearance. A few minutes later a small halo appeared around this white lesion; the halo was less dense and more yellowish in color than the lesion. Over the next three or four days the central bright area became smaller. A slight

vitreous haze was seen sometimes immediately after exposure but this usually disappeared on the third to fourth day. After four to five days, fine granules of pigmentation were visible around the burn and eschar formation took place much in the same manner as in a retinochoroidal inflammatory lesion or in an electric current induced diathermy puncture.

In the motion picture, the first few frames showed the illuminated area on the fundus. Then, usually in an area below the center, there appeared the white blanching of the coagulated tissue. This area spread constantly during exposure and at the end of a one-sec. exposure it usually exceeded the originally illuminated area.

With exposure times from 40 to 250 m. sec., clinically less severe lesions were observed. The color of these lesions was yellow rather than white and in the short exposure time (40 to 100. m. sec.), the lesion only appeared after two to three minutes in much the same manner as the halo around the more severe burns; also the shape of these lesions was different from the more severe burns, for they were kidney- or bean-shaped because of the image of the carbon holder on the retina. Presumably, conduction of heat into the shadow area took place only partially during these short exposures.

The clinical course of these mild lesions was very much the same as that of the big ones, pigmentation and, ultimately, scarification taking place four to 14 days after exposure. There was no noticeable change in appearance of these lesions after two weeks when they were usually barely visible; follow-up periods were terminated four to five weeks after exposure.

PATHOLOGY AND HISTOLOGY OF THE LESION

Routine celloidin sections and hematoxylin-eosin stains of exposed rabbit globes were examined microscopically. These globes were examined at various intervals after the burn exposure. A number of globes that received exposures from 500 to 1,000 milli-

seconds in our experiments with fundus motion picture photography were used for histologic studies. In these globes, enucleated and fixated immediately after the burn (within five to 10 minutes), the burn in the retina is readily seen in the sections (fig. 4). There is moderate swelling of the nerve-fiber layer and marked pyknosis of all the nuclei in the inner and outer nuclear layers. In the ganglion-cell layer, the cells appear structureless and show pyknotic or no nuclei. The structure of rods and cones is lost or modified in the burned area. The nuclei in the pigment epithelium showed marked pyknosis, fragmentation, or chromatolysis. There are little or no changes in the choroid immediately after burn.

In sections of eyes enucleated three or four days after burn, the changes in the retina were not much different from those already described; there was marked choroidal hyperemia but very little leukocyte infiltration around the burn. In several severe burns produced by one-second exposures, the inner layers of the sclera suffered, appearing homogeneously red and without nuclei in the area underlying the burn. Moderate pigment proliferation at the edges was

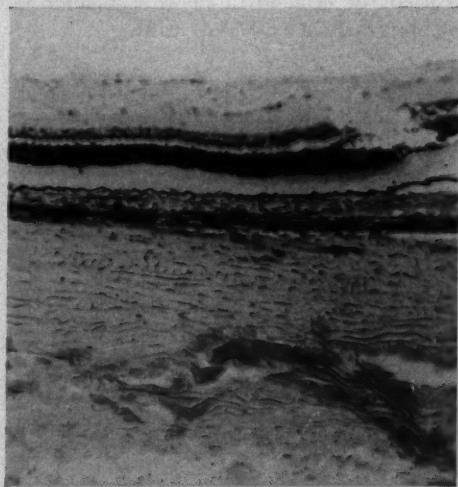


Fig. 4 (Ham, *et al.*). Moderate swelling of the nerve-fiber layer.

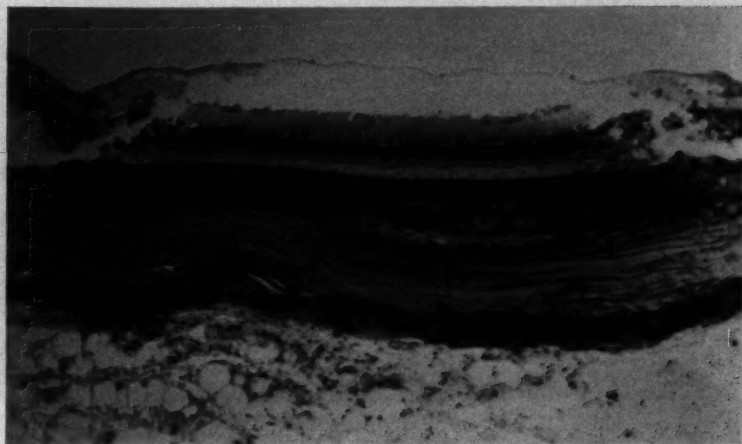


Fig. 5 (Ham, et al.). Moderate pigment proliferation.

seen in some sections as early as four days after exposure (fig. 5).

The few sections that we have obtained so far of lesions produced with exposure times from 50 to 100 milliseconds show a very similar picture (figs. 6 and 7). The damage seems to be confined mostly to the pigment epithelium, rods and cones, and the inner nuclear layer of the retina. The rod-and-cone layer shows a dark-red appearance and structures can be made out only vaguely. The outer nuclear layer in these mild lesions

is grossly disarranged, most of the nuclei being pyknotic. There is space formation in this layer causing the retina to bulge slightly outward. The other retinal layers show no, or only mild, cellular changes, the nerve-fiber and ganglion-cell layers appearing normal.

No follow-up histologic slides on these short exposure burns are available, as yet. The histologic appearance of the lesions produced in this laboratory is very similar to that described by Verhoeff and Bell.¹

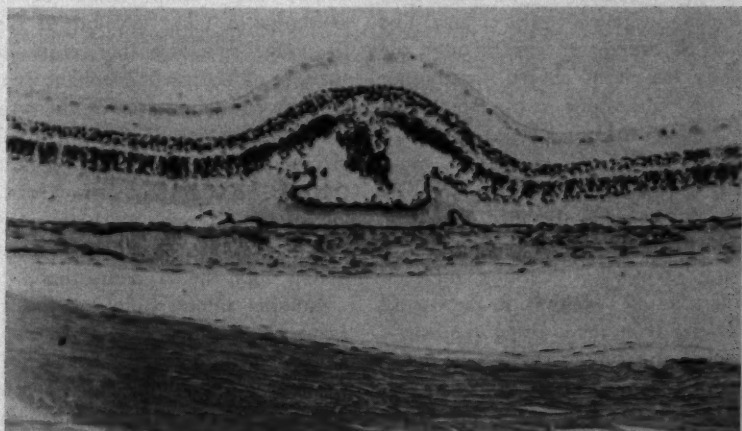


Fig. 6 (Ham, et al.). Damage seems to be confined mostly to the pigment epithelium.

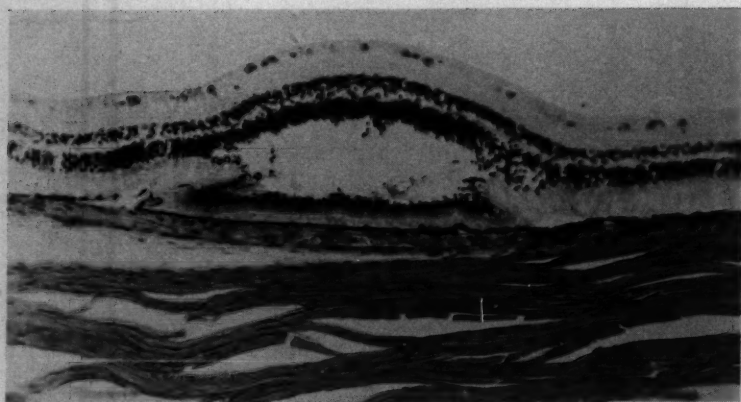


Fig. 7 (Ham, *et al.*). Exposure time 50 to 100 milliseconds.

EVALUATION OF THERMAL DOSE AT THE RETINA

In order to calculate the thermal-dose incident on the retina, the following factors must be known: the thermal intensity incident on the cornea, the pupillary diameter, the average transmission coefficient through the optic media, the area of the image on the retina, and the exposure time.

Reliable data for the thermal intensity in cal./cm.²/sec. incident on the cornea were provided by the water calorimeter which was cross-calibrated against other laboratory standards. The pupillary diameter is defined accurately by means of an eight mm. limiting aperture adjacent to the cornea. The transmission of radiant energy through the ocular media has been shown in another study of this laboratory using the same strain of rabbits to be approximately 78 percent.⁸

In order to calculate the image area we have taken the average distance from the nodal points to the retina of the rabbit eye to be 10 mm. Knowing the solid angle of the incident cone of radiation on the cornea and the distance from the limiting diaphragm to the cornea, one can calculate the image diameter produced on the retina.

The greatest source of error in this calculation is the distance from the nodal points

to the retina. This error has been minimized by carefully selecting animals with little variation in measurable ocular constants.

Fundus photography of the illuminated cone of radiation on the rabbit retina under the same experimental conditions provided an accurate check on this method of determining image size. The following formula for calculating the retinal thermal dose is used:

$$\frac{\text{cal./cm.}^2/\text{sec. at cornea} \times (\text{pup. diam.})^2 \times \text{transmission coeff.} \times \text{exp. time in seconds}}{(\text{true image diam.})^2 \times (\text{image shape factor})}$$

The image shape factor of 0.82 in the denominator takes account of the decrease in image area on the retina due to the shadow of the carbon holder. It is essential that the irradiated area on the retina be used and not the size of the burn lesion as determined subsequently by ophthalmoscope, fundus photography, or gross anatomic measurement, since we have noted that the size of the burn lesion depends to a marked extent upon the exposure time.

Fundus photography at the rate of 70 frames/sec. during the burn exposure was employed as one means of determining the thermal energies needed to produce irreversible retinal lesions. Blanching of the retina as seen after several exposed frames

was taken as a criterion for an irreversible lesion.

Table 1 summarizes the data obtained on 10 animals, six gray and four black rabbits. The lowest values were obtained with 4.5-inch limiting aperture producing a 1.1-mm. image diameter and ranged from 2.8 to 5.1 cal./cm². The average thermal dose for 14 burns on 10 animals was 3.6 ± 0.7 cal./cm². For the 3.0-inch aperture producing an image diameter of 0.7 mm. the average thermal dose was 4.9 ± 1.3 cal./cm², while the 1.625-inch aperture, producing an image diameter of 0.4 mm., required an average dose of 5.6 ± 1.3 cal./cm². These figures show that the thermal dose required for a thermal lesion increases markedly as the retinal image size decreases. This is probably due to increased conduction in the smaller lesion as previously noted by Verhoeff and Bell in 1916.¹

The production of minimal lesions in exposure times of 40 to 100 milliseconds has led us to question the validity of the motion-picture photography technique to determine the thermal energy to produce a minimal irreversible lesion. It is also a matter of sub-

TABLE 1
SUMMARY OF BURN DATA OBTAINED BY FUNDUS PHOTOGRAPHY

| Rabbit No. | 4.5-inch Aperture Thermal Dose cal./cm. ² | 3.0-inch Aperture Thermal Dose cal./cm. ² | 1.625 inch Aperture Thermal Dose cal./cm. ² | 1.0-inch Aperture Thermal Dose cal./cm. ² |
|------------|--|--|--|--|
| 135B | 3.8 | — | — | — |
| 136B | 3.0 | 5.5 | 5.7 | — |
| 136B | 4.5 | — | — | — |
| 145G | 3.5 | 5.5 | — | — |
| 144G | 2.8 | 4.0 | 4.0 | — |
| 140G | 3.1 | 3.0 | 5.1 | — |
| 141G | 4.1 | — | 3.9 | — |
| 141G | 4.0 | — | — | — |
| 141G | 3.0 | — | — | — |
| 129G | 3.0 | 5.1 | 6.5 | 9.0 |
| 130B | 3.0 | 4.4 | 6.3 | — |
| 130B | — | 4.5 | — | — |
| 126G | 3.5 | 7.4 | 7.9 | — |
| 131B | 3.4 | — | — | — |
| 131B | 5.1 | — | — | — |
| Av. | 3.56 ± 0.65 | 4.93 ± 1.33 | 5.63 ± 1.32 | 9.0 |

TABLE 2
PRELIMINARY BURN DATA BY SHORT EXPOSURE TIME TECHNIQUE
(Using the 4.5-inch diameter limiting aperture)

| Rabbit No. | Exposure Time in Seconds | Thermal Dose in cal./cm. ² | Burn |
|------------|--------------------------|---------------------------------------|------|
| 141G | 0.0551 | 2.40 | No |
| 141G | 0.0652 | 2.86 | No |
| 141G | 0.1061 | 4.68 | Yes |
| 144G | 0.0649 | 2.73 | No |
| 144G | 0.0590 | 2.48 | No |
| 144G | 0.0829 | 3.47 | Yes |
| 144G | 0.0825 | 3.46 | Yes |
| 145G | 0.0902 | 4.26 | Yes |
| 145G | 0.0717 | 3.38 | Yes |
| 145G | 0.0491 | 2.32 | Yes |
| 145G | 0.0487 | 2.30 | No |
| 135B O.S. | 0.0267 | 1.25 | No |
| 135B O.S. | 0.0483 | 2.19 | Yes |
| 135B O.S. | 0.0685 | 3.09 | Yes |
| 135B O.S. | 0.0664 | 3.00 | Yes |
| 135B O.D. | 0.0961 | 4.34 | Yes |
| 135B O.D. | 0.0672 | 3.05 | Yes |
| 135B O.D. | 0.0500 | 2.26 | No |
| 135B O.D. | 0.0490 | 2.21 | No |
| 135B O.D. | 0.0919 | 4.15 | Yes |

Average for lowest "Yes" value of each eye— 3.14 ± 0.81 .
Standard Deviation—0.81.

jective judgment to decide just at which frame the first signs of blanching occur. Accordingly, we have abandoned the fundus motion-picture photography method in favor of the more difficult but sensitive method of varying the exposure time from burn to burn and waiting several minutes to evaluate the result of the exposure. This method involves a hit-and-miss technique which is ideally suited to the type of statistical analysis known as the Probit method. We still employ the fundus camera, however, to align the eye properly.

In Table 2 are summarized a limited number of short exposure experiments on four animals, placing several burns on each eye. Success or failure to produce an observable lesion after waiting at least five minutes is indicated in the column under *burn* by yes or no. In these experiments only the 4.5-inch limiting aperture has been used to date. The lowest thermal dose which has produced an

observable lesion is 2.2 cal./cm². Most of the minimal lesions observed required 3.0 to 4.0 cal./cm², which is in the same range as deduced by the fundus photography method.* Nonetheless it seems preferable to depend on the statistical method for further evaluation of threshold and reciprocity since it is inherently more sensitive.

SUMMARY

a. A technique has been evolved in this laboratory for the production and study of small retinal burns in rabbit eyes. A 24-inch carbon-arc searchlight equipped with

an aluminized ellipsoidal mirror has been utilized as the source of radiation. A second ellipsoidal mirror is used to reduce the angle of convergence of the radiation in order to simulate the fireball of an atomic weapon viewed at appreciable distances. Intensities of 1.2 to 1.4 cal./cm²/sec. as measured by a waterflow calorimeter are available at the cornea of the rabbit eye. Provision is made for motion-picture photography of the burn.

b. The ophthalmoscopic and histologic appearance of lesions produced by various exposure times are described. Two methods of evaluating the thermal dose for a minimal irreversible retinal lesion are compared. The dose for such a lesion is a function of retinal image size during the burn. Up to the present, the dose required to produce a minimal burn lesion in the rabbit retina has been found to range between 2.0 and 4.0 cal./cm².

* Recent and more accurate determinations by the Probit method indicate that the thermal threshold for minimal lesions ranges from 0.8 to 1.1 cal./cm². This is considerably below the threshold determined by fundus photography.

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THE CHAMBER ANGLE IN INTERSTITIAL KERATITIS*

REPORT OF A CASE

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Although interstitial keratitis associated with congenital syphilis used to be a common disease in earlier decades and was much more general than now, pathoanatomic investigations on this condition have been published to a very insignificant extent. This of course was mainly due to the fact that the disease is not fatal in itself. It is all the more significant that almost all histologic examinations have revealed changes in the chamber angle. Biomicroscopic examinations of the chamber angle in this disease have been published to an even lesser extent.

REVIEW OF THE LITERATURE

In the pathoanatomic study published by v. Hippel⁶ the patient was a boy, aged 15 years, who had been affected with interstitial keratitis during the previous year. Examination revealed that the chamber angle was almost completely closed. In Elschnig's⁸ case, a girl, aged eight years, died during the course of acute interstitial keratitis. Histologic examination showed, in the region of ligamentum pectinatum, a strong infiltration of leukocytes which continued up to the ciliary body.

In the case published by Watanabe¹³ keratitis had been present six months before examination. At the chamber angle and around Schlemm's canal, a cell infiltration was seen, which in part penetrated into the corneal parenchyma.

Kunze's⁸ publication concerned healed keratitis. Infiltration stretched from the chamber angle to the ciliary body. In Jaeger's⁷ investigation, reporting a patient who had had interstitial keratitis for the duration of half a year, the region of the liga-

mentum pectinatum and of the ciliary body showed infiltrations of round cells.

Seefelder's¹³ patient died during acute keratitis. In the chamber angle and the corneoscleral meshwork there were abundant accumulations of exudate cells with lobular and round nuclei. Bentele's¹ patient also died during the course of interstitial keratitis. The round cell and leukocyte infiltration which was present in the region of the ligamentum pectinatum extended as far as the ciliary body.

Particular interest and significance are attached to the observations of Friedenwald⁴ made in the course of his histologic examinations of syphilitic babies who were either stillborn or had died during the early neonatal period. Friedenwald frequently found infiltrations in the iris, chamber angle, and ciliary body with distinguishable mononuclear cells, lymphocytes, and myeloid cells. According to this author, iridocyclitis so slight usually as to produce no clinical symptoms, was not uncommon in fetal syphilis.

I failed to find any references to biomicroscopic examinations of the chamber angle during the acute stage of interstitial keratitis. In one of my previous investigations⁹ I found, at a gonioscopic follow-up, pathologic changes in the chamber angle of 13 eyes out of 17. The changes were mostly revealed as ciliary and trabecular synechias, as well as increased pigmentation. No correlation could be established between haziness of the cornea and changes in the chamber angle.

It is surprising that so little attention has been given to histologic and biomicroscopic changes in the chamber angle, particularly since several authoritative investigators have underlined the limbal or scleral onset as being typical of the disease. Vogt,¹⁶ when following a case from the very beginning, saw through

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the slitlamp as a beginning change a limbal opacity of Descemet's membrane. In another case, Vogt saw the first changes in the sclera close to the limbus. According to Igerscheimer,⁸ the disease often starts at the corneal margin but may also be manifested by symptoms of episcleritis.

CASE REPORT

I shall describe below a patient treated by me for interstitial keratitis, in whom it was possible to examine the chamber angle gonioscopically in the acute stage of the disease. Since I have not found any previous publications of corresponding observations, and since my own observations bear out to some extent my previously published views on the nature of interstitial keratitis (Oksala¹⁰), I feel this case merits recording.

Patient T. S. (hospital record 7958/55), a girl, aged eight years, came to the Ophthalmological Department for treatment on November 28, 1955, complaining of sensitivity to light and impaired acuity of vision in the right eye of two weeks' duration.

The patient's parents stated that they had always enjoyed good health. The patient had not previously suffered from any diseases worth mentioning. There was no history of eye diseases in the patient up to now.

The general condition of the patient was good. Apart from the eye changes, clinical and roentgenologic examinations failed to produce any symptoms of congenital syphilis. SR was 12 mm./hour. Alb. —, Nyl. —, WaR +, cholWaR +, Kahn +, and Sitolipin +. No pathologic changes were found on roentgenologic examination of the thorax.

Ophthalmologic examination on November 28, 1955 showed:

Right eye. Vision: 1.0, right projection. Tension: 18 mm. Hg (Schiotz). The lids were swollen, with blepharospasm. Severe ciliary congestion was present in the eye. The cornea was edematous and revealed infiltrates on an extensive area; they were located both in the central parenchymal parts and on a deeper level close to Descemet's

membrane. In two places on the corneal margin the superficial blood vessels penetrated into the cornea in a broomlike formation. The posterior surface showed precipitates with a ring-shaped organization. The aqueous flare was visible, +2. The iris was hyperemic, +2. The deeper parts of the eye were indistinguishable.

Left eye. Vision: 1.3, emmetropic. Tension: 20 mm. Hg (Schiotz). The anterior portion of the eye was symptom free. The transparent parts were clear. The eyegrounds exhibited typical "pepper and salt" changes which were most pronounced on the periphery.

Gonioscopic exploration with Goldmann's lens (fig. 1-B). The chamber angle had normal depth. Pathologic changes were visible in every direction. There were abundant pigmentation particles and trabecular synechias in the trabecula sclerae. Schlemm's canal was not discernible. The ciliary process was only visible in places. A fairly large blood vessel was seen in two places to emerge from the ciliary body and to pass over the trabecula sclerae for a short distance into the cornea. Apart from synechias, the iris was asymptomatic.

Because of the congenital syphilis, the patient was given procaine penicillin at the rate of 600,000 units daily for 18 days. The right eye was treated locally with one-percent atropine drops, three times daily, and 2.5-percent hydrocortone drops every hour.

After one week of treatment congestion of the right eye disappeared, as did the corneal edema. Two small infiltrates and precipitates were visible in the middle of the cornea. Blood vessels could no longer be distinguished in the cornea.

Gonioscopic examination made at that time gave the following results (fig. 1-A):

The chamber angle had normal depth. Pathologic changes were seen everywhere. The trabecula sclerae had abundant particles of pigmentation and trabecular synechias. A dilated iritic blood vessel was visible at the bases of the broader synechias. While the

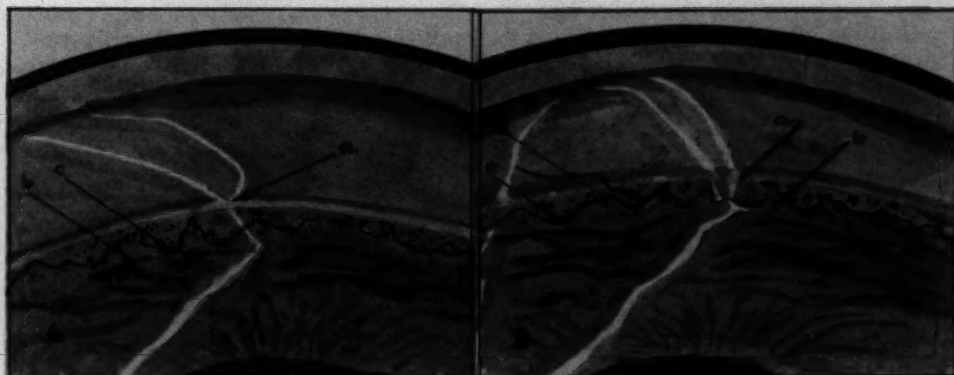


Fig. 1 (Oksala). Gonioscopic view of (A) the right and (B) the left eye. (a) The line of Schwalbe. (b) A trabecular synechia at the base of which, in the right eye, a dilated iritic blood vessel is visible. (c) Ciliary body band. (d) A blood vessel which emerges from the ciliary body and passes over the scleral trabecula and proceeds for a short distance into the cornea.

pupillary part of the iris was symptom-free under routine examination with a slitlamp, the ciliary part still revealed marked hyperemia when examined gonioscopically. Schlemm's canal was not visible, whereas the ciliary process could be discerned in places.

After a treatment of about four weeks' duration, the symptoms in the right eye subsided completely. The changes visible in the chamber angle were fairly similar at the time to those seen in the left eye.

DISCUSSION

The patient had typical interstitial keratitis in the right eye. As a result of local hydrocortone therapy, corneal opacities were soon cleared up, beginning from the surface and then deeper down. The precipitates began to disappear, at first on the periphery and lastly from the central part of the cornea. The superficial blood vessels which had been visible at the margins, completely disappeared. Formations of deeper vessels did not occur.

It is particularly typical of interstitial keratitis that superficial corneal changes, infiltrations, and vessels disappear more rapidly and completely than deeper ones which are located in the vicinity of Descemet's membrane. The superficial vessels, which

occur in the initial stages of the disease and form a broomlike pattern near the limbus, emerge mainly from the conjunctiva and the episclera. There is a later formation of deeper vessels which spread in different directions within the cornea, emerge from the sclera and, according to my gonioscopic observations, also from the ciliary body.

When the right cornea had become much more transparent, it was possible to examine the chamber angle gonioscopically. The most pronounced changes then seen were abundant trabecular synechias, in the broader bases of which the dilated iritic vessel could be clearly noted. Increased pigmentation was present in the trabecula.

Hyperemia of the iris was most pronounced at the periphery and it may have partly contributed toward the occurrence of extension of the synechias. Hyperemia of the iris disappeared first from the pupillary and lastly from the ciliary part.

It is possible that synechias in particular serve to increase irritation and congestion of the iris. Perhaps this circumstance plays some part in the easily recurring character of the disease. It should then be borne in mind that synechias may be a remnant of fetal iridocyclitis, which is possibly indicated by the observations I made in the left eye.

The longer persistence of peripheral hyperemia of the iris is certainly also affected by the proximity of the ciliary body and by the circumstance that the reducing influence of mydriatics upon the surface of the iris is most pronounced in the pupillary part. So far the significance of these synechias in interstitial keratitis and other inflammatory conditions of the eye and their after-effects has scarcely been investigated.

According to the history given by the parents and the patient, the left eye had always been healthy. On admission the anterior part of the eye was found to be a symptomatic on routine slitlamp examination. The eye fundi revealed typical "pepper and salt" changes.

Gonioscopic examination showed the changes already referred to, which were reminiscent of the observation made by Friedenwald several years ago and called to mind his statement that iridocyclitis was not uncommon in fetal syphilis. It is therefore possible that the patient treated by me may have had cyclitis as early as in fetal life, the marks of which were the persistent changes observed in the chamber angle.

How great a role these changes may have played in the onset of interstitial keratitis at a later age, should, in the light of this single case, be left to conjecture. In any event, and on the basis of Friedenwald's observations and my own, one can postulate that final proof is lacking for the widespread opinion that interstitial keratitis occurs primarily in the cornea, under the influence of either spirocheta (Igersheimer⁶), antibodies (Schieck¹¹), species foreign protein (v. Szily¹⁴), or some toxin (Schultze¹²).

In a previous paper¹⁰ I established that eyeground changes occurred in the active stage of interstitial keratitis. On the basis of

this, my earlier observations,⁹ and the patho-anatomic changes reported in the literature, the possibility was suggested that interstitial keratitis might involve some kind of panophthalmitis, an opinion expressed in their time by Stellwag von Carion² und v. Hippel,⁸ and others. The gonioscopic observations herein described provide support for this assumption about the nature of the disease.

SUMMARY AND CONCLUSIONS

Marked changes in the chamber angles are almost invariably reported in pathoanatomic studies on interstitial keratitis published in the literature. Biomicroscopic observations also suggest the significance of chamber-angle changes in the genesis of interstitial keratitis.

I was able to study the chamber angle of a patient suffering from interstitial keratitis associated with congenital syphilis during the active stage of this disease. Trabecular synechias and increased pigmentation were visible in the affected eye. In the course of the disease, hyperemia of the iris disappeared first from the pupillary and only much later from the ciliary part. The other eye, which had a history of previous health and was clinically asymptomatic, also showed in its chamber angle abundant trabecular synechias, increased pigmentation, and two blood vessels which emerged from the ciliary body and, having passed over the trabecular sclera, ran for a short distance within the cornea.

I consider it possible that iridocyclitis which had occurred either in fetal or early neonatal life may be a contributing factor in the genesis of interstitial keratitis. The formation of trabecular synechias might promote the onset of interstitial keratitis and its later recurrences.

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BILATERAL METASTATIC CARCINOMA TO CHOROID AND OPTIC NERVES*

WITH HEMORRHAGE INTO ONE OPTIC NERVE: A CLINICOPATHOLOGIC CASE REPORT

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A case of bilateral metastatic carcinoma to the choroid and to the optic nerve is of sufficiently rare occurrence to warrant this report. Because of extensive retinal detachments, no ophthalmoscopic diagnosis could be made. In spite of repeated and thorough physical examinations, the primary carcinoma of the breast was discovered only several months after appearance of the initial eye symptoms.

CASE REPORT

Mrs. M. R., a 71-year-old white woman, was referred to one of us (D. S.) because of failing vision in both eyes. Her history revealed that the vision in her right eye began to fail in March, 1955. She was told that she had a "hemorrhage" in the right eye. No details concerning this examination could be obtained.

She consulted an ophthalmologist on May

13th. At that time the right vision was nil, the left vision was 6/45. There was a minimal retinal detachment in the right inferior temporal quadrant. No lesion could be seen in the left eye to account for the loss of vision. Six weeks later, there was a bilateral minimal detachment in both inferior temporal quadrants. Physical examination, neurologic examination, and X-ray films of the skull were noncontributory.

During her first visit on July 25, 1955, the vision in both eyes was limited to recognition of hand movements. The patient did not complain of ocular pain at any time.

There was an enormous bilateral detachment of the retinas, perhaps more extensive in the right eye. The detachments were limited to the floor and sides of each globe; the roofs were intact. There were no holes or disinsertions. There was no evidence of inflammation—not even the slightest vitreous haze.

On the basis of the bilaterality, a tentative diagnosis of exudative detachment (possibly Harada's disease) was made. The patient

*From the Department of Ophthalmology, The Northwestern University Medical School. Presented before the Chicago Ophthalmological Society, October 1, 1956.

was hospitalized on August 1st. Two weeks of absolute bedrest and bilateral occlusion failed to cause any change in the appearance of the detachments. Another physical examination was again noncontributory. The patient's age, the failure of the detachments to flatten on bedrest, and the absence of retinal breaks prompted the decision against surgery.

During the next few months, the general condition of the patient deteriorated. A small mass was found in the left breast which was amputated in October, 1955. On November 3rd, the physician who had originally referred the patient reported that he had found metastases in the lung.

The patient died on January 11, 1956.

PATHOLOGIC REPORT

Autopsy revealed multiple metastases in both lungs, in the posterior cul-de-sac, in the

peritoneum, and in the anterior mediastium. Only one very small metastasis was found in the liver (Dr. Ruth Balkan, Evanston Hospital).

Both globes were imbedded in nitrocellulose. Serial meridional sections were performed. A description of the anterior segments would add nothing to the discussion of the case.

Except for its attachment at the ora serrata and the disc, the right retina is detached by pale staining, amorphous, pinkish material that contains no formed elements.

The choroid, for the most part, is replaced by a tumor that extends temporally to the ora serrata, but only three mm. to the nasal side (fig. 1). One of the scleral channels, possibly that of a short posterior ciliary artery, is enormously distended and filled by a tumor mass extending from the outside of the sclera into the main body of the tumor

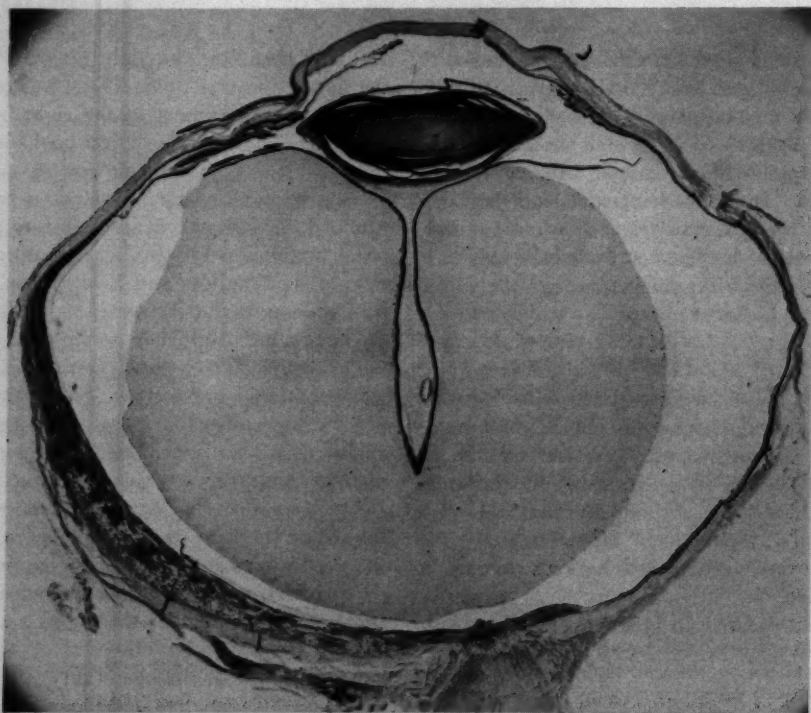


Fig. 1 (Van Wien and Shoch). Right eye. Mushroom-shaped retinal detachment. Metastatic carcinoma involving choroid mostly on temporal side but extending to nasal side for a distance of three mm. ($\times 6.3$).

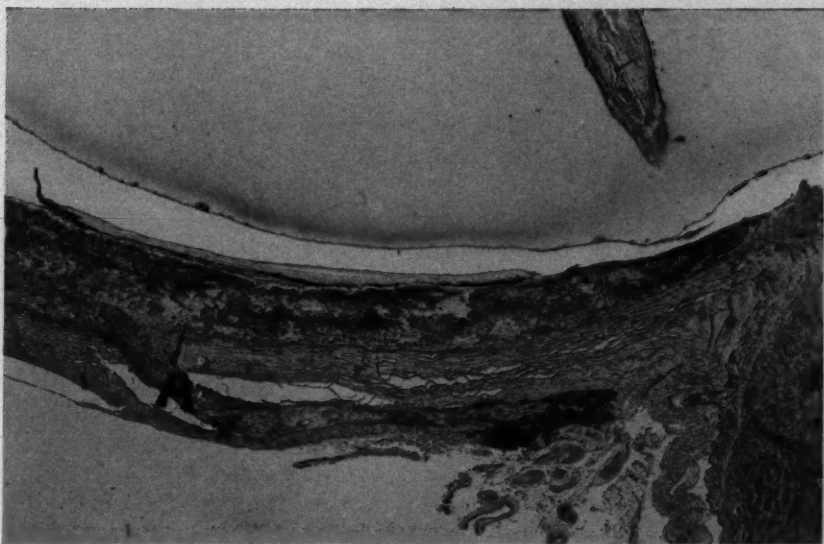


Fig. 2 (Van Wien and Shoch). Tumor (A) extending from outside of globe through scleral channel into main body of choroidal metastasis ($\times 14$).

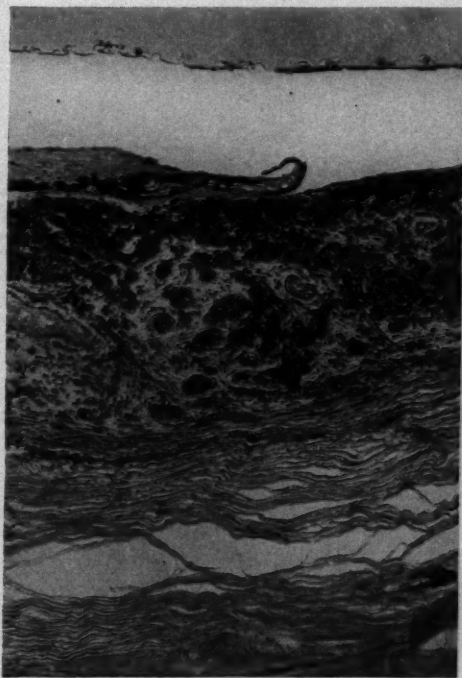


Fig. 3 (Van Wien and Shoch). There is a conspicuous lack of stroma ($\times 60$).

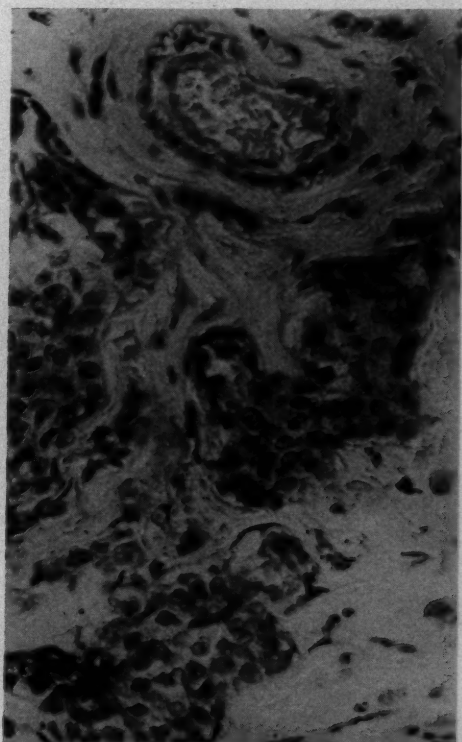


Fig. 4 (Van Wien and Shoch). Higher magnification of Figure 3 ($\times 390$).

(fig. 2). A conspicuous lack of stroma makes it quite impossible to be specific as to the nature of the primary tumor (fig. 3).

The cytologic elements of the tumor are pale, large cells that show irregular shape and size. There are quite a number of irregular mitotic patterns (fig. 4).

Nests of tumor cells occupy the prelaminar portion of the optic nerve. Isolated tumor cells have invaded the retrolaminar portion of the optic nerve for a distance of one mm. This area comes to an abrupt end because, for a distance of about two mm., an area of fresh hemorrhage is noted in the optic nerve, with no neural or tumor elements in evidence (fig. 5 and fig. 6).

Behind this hemorrhagic area, the nerve fibers are replaced by tumor cells between

intact septa (fig. 7). However, in some areas, erythrocytes are seen in addition to tumor cells. These tumor cells stain much less vividly than those in the choroid and the distal part of the nerve; in some nests, they are completely necrotic, giving the appearance of ghost cells.

There is a moderate infiltration of the subarachnoid space by tumor cells. There is no trace of a hemorrhage into the subarachnoid space.

The left eye shows a retinal detachment similar to that of the right eye (fig. 8). There is also a metastatic carcinoma of the choroid that extends for seven mm. to the nasal side, and well into the pars plana of the ciliary body on the temporal side. The appearance of the tumor is quite similar to



Fig. 5 (Van Wien and Shoch). Infiltration of prelaminar portion of optic nerve. Isolated tumor cells extend into the distal end of the retrolaminar portion. This area is interrupted abruptly by a hemorrhage into the optic nerve. The proximal end shows areas of necrosis ($\times 22.3$).

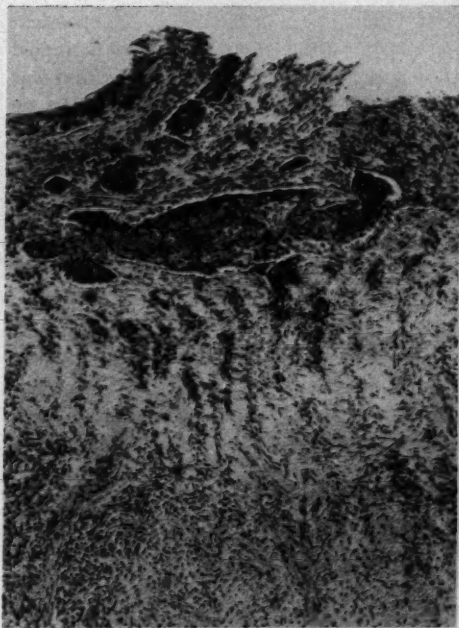


Fig. 6 (Van Wien and Shoch). Higher magnification of distal end of optic nerve ($\times 90$).



Fig. 8 (Van Wien and Shoch). Left eye. Retinal detachment similar to the one in right eye with metastatic carcinoma of choroid extending into optic nerve ($\times 6$).

that in the other eye except for the appearance of fairly distinct alveoli in some areas (fig. 9 and fig. 10). The left optic nerve is invaded by the tumor which extends uninterruptedly from the choroid to the proximal end of the nerve (fig. 11). The tumor cells, within the nerve, have a distinct alveolar

pattern. There is a minimal infiltration of the subarachnoid space.

COMMENT

The most unusual feature of this case is the loss of vision in the right eye which preceded equivalent ophthalmoscopic findings by

Fig. 7 (Van Wien and Shoch). Higher magnification of proximal end of optic nerve ($\times 130$).



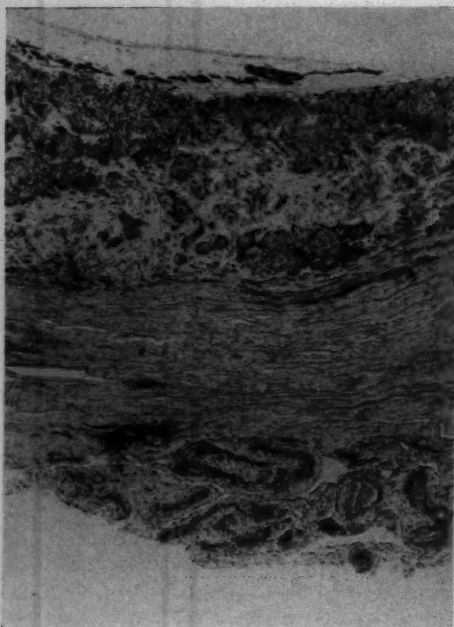


Fig. 9 (Van Wien and Shoch). Tumor showing alveolar pattern in some areas ($\times 57.5$).

several months. The minimal detachment could have hardly accounted for complete loss of vision.

Metastatic carcinomas to the choroid are not too infrequent, with bilaterality reported in the literature in 20 to 25 percent of cases (Cordes,¹ Cohen,² Lemoine and McLeod,³ Ginsberg⁴). Metastases to the optic nerve, on the other hand, are extremely rare. Behr⁵ is of the opinion that only the cases reported by Holden, Krohn, Elschmig, and Ginsberg are true instances of metastases to the optic nerve that did not extend into the choroid. To this small group Terry's⁶ case should be added. Undoubtedly, there must be a great number of instances where metastases to the choroid extended into the optic nerve. On the contrary, cases of metastases to the optic nerve with extension into the choroid seem to be extremely rare. The case of McDannald and Payne⁷ as well as that of Cords⁸ are cited as examples for that occurrence.

Another possibility, finally, is a metasta-

sis to the optic nerve and an independent metastasis to the choroid. The only report of such a case that we were able to find was that of Behr.⁵ He based his conclusion on the appearance and staining properties of the tumor cells which were quite small and stained poorly in the choroid but stained much better in the optic nerve.

It seems quite possible that the case under discussion can be cited as another instance of metastasis to the right optic nerve and an independent metastasis to the choroid. The appearance of the tumor cells would suggest that involvement of the right optic nerve occurred first. This affords a perfectly satisfactory explanation for the loss of vision without ophthalmoscopic findings.

The picture is somewhat complicated by the hemorrhage into the nerve. Though the hemorrhage seems to be of a somewhat recent origin, the pressure of the extravasation, nevertheless, could have caused necro-

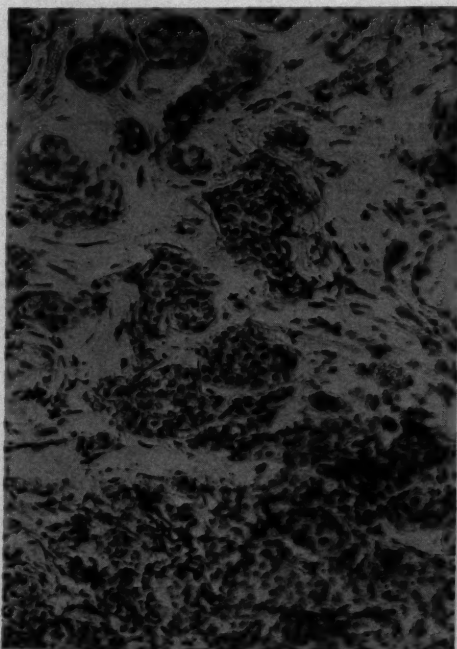


Fig. 10 (Van Wien and Shoch). Higher magnification of Figure 9 ($\times 190$).



Fig. 11 (Van Wien and Shoch). Tumor invading optic nerve shows alveolar pattern ($\times 50$).

sis of the tumor cells. Needless to say, a hemorrhage into the optic nerve is exceedingly rare. Scharizer⁹ found a traumatic arteriovenous aneurysm of the optic nerve in which the extravasated blood had eroded a cavity in the substance of the optic nerve. Our case seems to be the first in which a tumor caused involvement of a central retinal vessel with subsequent hemorrhage into the nerve.

Bilateral retinal detachment, especially in cases of known primary carcinoma, should always arouse suspicion of metastatic car-

cinoma of the choroid. Yet, in our case, repeated physical examinations did not reveal the primary tumor. Even today it is not unusual to find instances in which the tumor of the eye (sometimes after enucleation) is the first manifestation of a general carcinomatosis, or at least of a primary tumor situated elsewhere. Reese¹⁰ added four of his own cases to the literature. However, his were cases with primary carcinomas of the lung, the thyroid gland, and the stomach (with one case of unknown primary site). Such tumors are much more difficult to discover than a

tumor of the breast. Our case certainly is unique for there were ocular symptoms eight months before the primary tumor was discovered in spite of repeated physical examinations.

SUMMARY

A case with bilateral choroidal metastatic carcinoma with involvement of the optic

nerves is presented. In addition, there is an independent metastasis to one nerve complicated by a hemorrhage into the nerve. Ocular symptoms occurred eight months before the primary breast tumor could be discovered.

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REPORT OF A NEW CARBONIC ANHYDRASE INHIBITOR (SQUIBB-MC-9367)*

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In 1950 the heterocyclic sulfonamides were reported as carbonic anhydrase inhibitors by Miller, Dessler, and Roblin.¹ One of these, Diamox (2-acetylalmino-1,3,4-thiadiazole-5-sulfonamide) continues to be investigated. This preparation has proved to be an effective agent in lowering the intraocular pressure in humans.

Another compound of a similar nature has

been developed at the Squibb Institute for Medical Research. This preparation, which is a propanyl derivative of Diamox, is known as Squibb N (5-sulfamoyl-1,3,4-thiadiazole-2-YL) propionamide. It is also called MC-9367).²

In trials on laboratory animals³ it has been shown to have a diuretic effect following its oral administration to normal hydrated dogs. These test dogs excreted as much urine and sodium following oral doses with MC-9367 as they did following doses with acetazolamide. MC-9367 caused no greater excretion of potassium than did acetazolamide (Diamox).

*From the Ophthalmological Service of the Philadelphia General Hospital, Blockley Division. The drug tested was supplied through the courtesy of H. A. Strade, of E. R. Squibb & Sons. The opinions expressed herein are those of the authors and do not represent the opinions of the Navy Department or the United States Government.

TABLE 1
CONTROL GROUP

| No. | Age (yr.) | Eye | (mm. Hg, Schiøtz) | | | | | |
|-----|--------------|---------------------|-------------------|----------|----------|----------|----------|-------|
| | | | Prior | 0.5 hr. | 1 hr. | 2 hr. | 4 hr. | 6 hr. |
| 1 | 40 | OD OS | 15 15 | 17 17 | 15 15 | 15 14 | 12 12 | |
| 2 | 40 | OD OS | 20 22 | 20 20 | 17 15 | 15 15 | 15 15 | |
| 3 | 60 | OD OS | 22 22 | | | 13 14 | | |
| 4 | 61 | OD enucleated OS | 18 | 15 | 15 | 15 | 15 | |
| 5 | 25 | OD OS | 19 20 | 15 20 | 17 20 | 15 19 | 15 19 | |
| 6 | 17 | OD OS | 19 19 | 18 18 | 16 18 | 16 15 | 16 15 | |
| 7 | 22 | OD enucleated OS | 20 | 15 | 15 | 18 | 15 | |
| 8 | 28 | OD OS | 15 18 | 15 15 | 15 15 | 12 14 | 12 12 | |
| 9 | 40 | OD OS | 20 18 | 16 15 | 15 12 | 14 14 | 12 14 | |
| 10 | 22 | OD OS | 23 23 | 20 20 | 18 18 | 15 15 | 14 15 | |
| 11 | 25 | OD OS | 20 20 | 20 20 | 15 15 | 15 12 | 14 14 | |
| 12 | 45 | OD OS | 22 26 | 23 23 | 23 23 | 20 20 | 12 13 | |
| 13 | 30 | OD OS | 20 20 | 14 15 | 15 15 | 14 15 | | |
| 14 | 15 | OD phthisis OS | 20 | 20 | 18 | 12 | 12 | |
| 15 | 77 | OD enucleated OS | 23 | 18 | 18 | 14 | 15 | |
| 16 | 38 | OD enucleated OS | 18 | 15 | 18 | 15 | 14 | |
| 17 | 75 | OD enucleated OS | 23 | 23 | 18 | 15 | 12 | |
| 18 | 65 | OD OS | 20 | 18 | 18 | 15 | 15 | |
| 19 | 55 | OD OS | 20 | 15 | 15 | 15 | 15 | |
| 20 | 47 | OD OS | 20 20 | 26 26 | 22 25 | 20 23 | 20 23 | |
| 21 | 56 | OD enucleated OS | 15 | 12 | 13 | 10 | 10 | |
| 22 | 46 | OD OS | 20 | 17 | 15 | 16 | 16 | |
| 23 | 45 | OD OS | 23 23 | 18 20 | 15 18 | 17 18 | 18 18 | |

PRESENT STUDY

1. CONTROL GROUP

Twenty-three patients with 40 eyes free of glaucoma were used as a control group at the Philadelphia General Hospital, Blockley Division. After recording their average normal intraocular pressures, they were each given a single oral dose of 500 mg. of MC-9367. Average readings were recorded at intervals of 0.5, one, two, four, and, in some cases, six hours. The 5.5-gm. and 7.5-gm. weights of a recently standardized Schiøtz tonometer were used by the same examiner throughout the study. The topical anesthetic agents used were tetracaine (0.5 percent) and Ophthaine. In a given patient, the same anesthetic agent was used for all tonometric readings.

From the tabulation of the results with the control group it was observed that there were decreases of 6.0 mm. Hg or more in the intraocular pressure of 18 eyes. Although the intraocular pressure actually decreased

in 39 of the 40 eyes observed, only a decrease of 6.0 mm. Hg or more was considered significant. None of these patients was receiving miotic therapy.

2. GLAUCOMA PATIENTS

Similar tonometric studies and observations were made on 30 known glaucoma patients, proven by repeated tonometric studies, field tests, and gonioscopic observations. These patients were from both the wards and the Glaucoma Clinic of the Philadelphia General Hospital, Blockley Division. These patients were likewise given a single oral dose of 500 mg. of MC-9367.

Table 2 shows the effect of the drug on 15 eyes of nine patients with narrow-angle glaucoma, who were on miotic therapy and had been previously controlled by combinations of Diamox and miotics. The Diamox therapy had been discontinued for one week prior to the administration of the drug, resulting in the elevation of the tensions, as

TABLE 2
NARROW-ANGLE GLAUCOMA

| No. | Age (yr.) | Eye | (mm. Hg, Schiøtz) | | | | | |
|-----|--------------|---------------------|-------------------|----------|----------|----------|----------|-------|
| | | | Prior | 0.5 hr. | 1 hr. | 2 hr. | 4 hr. | 6 hr. |
| 1 | 71 | OD OS enucleated | 38 | 38 | 33 | 33 | 27 | |
| 2 | 45 | OD OS | 38 23 | 30 18 | 20 15 | 14 20 | 15 18 | |
| 3 | 67 | OD OS | 49 40 | 27 30 | 20 18 | 20 18 | 18 18 | |
| 4 | 56 | OD OS | 45 45 | 33 35 | 33 28 | 27 28 | 23 20 | |
| 5 | 70 | OD OS | 33 29 | 20 29 | 33 27 | 25 23 | 25 18 | |
| 6 | 72 | OD OS | 53 20 | 49 15 | 50 19 | 35 14 | 26 12 | |
| 7 | 73 | OD OS | 80 80 | 55 49 | 60 60 | 45 33 | 30 35 | |
| 8 | 50 | OD OS iridectomy | 65 | 60 | 45 | 30 | 18 | 18 |
| 9 | 67 | OD OS phthisis | 49 | 49 | 35 | 27 | 27 | 33 |

TABLE 3
WIDE-ANGLE GLAUCOMA

| No. | Age (yr.) | Eye | (mm. Hg, Schiøtz) | | | | | |
|-----|--------------|-----|-------------------|---------|-------|-------|-------|-------|
| | | | Prior | 0.5 hr. | 1 hr. | 2 hr. | 4 hr. | 6 hr. |
| 1 | 41 | OD | 45 | 27 | 26 | 23 | 22 | 22 |
| | | OS | 38 | 33 | 19 | 17 | 18 | 18 |
| 2 | 68 | OD | 40 | 30 | 25 | 21 | 26 | 26 |
| | | OS | 20 | 22 | 15 | 14 | 14 | 14 |
| 3 | 56 | OD | 38 | 35 | 30 | 30 | 30 | |
| | | OS | 40 | 38 | 38 | 30 | 30 | |
| 4 | 72 | OD | 30 | 27 | 25 | 23 | 20 | |
| | | OS | 27 | 23 | 23 | 18 | 20 | |
| 5 | 45 | OD | 28 | 25 | 27 | 27 | 25 | |
| | | OS | 35 | 30 | 26 | 26 | 22 | |
| 6 | 60 | OD | 50 | 45 | 30 | 20 | 23 | |
| | | OS | 15 | 14 | 10 | 12 | 10 | |
| 7 | 72 | OD | 45 | 49 | 50 | 49 | 30 | |
| | | OS | 40 | 40 | 40 | 40 | 27 | |
| 8 | 58 | OD | 40 | 38 | — | 26 | 24 | |
| | | OS | 49 | 45 | — | 26 | 22 | |
| 9 | 50 | OD | 55 | 55 | 55 | 55 | 55 | |
| | | OS | 65 | 65 | 65 | 65 | 65 | |
| 10 | 68 | OD | 30 | 20 | 23 | 23 | 23 | |
| | | OS | 35 | 30 | 26 | 23 | 23 | |
| 11 | 70 | OD | 22 | 15 | 15 | 30 | 15 | |
| | | OS | 49 | 30 | 30 | 28 | 22 | |

noted in the "Prior" column in Table 2. This group showed significant reduction in the tension in every case of glaucoma, as well as reduction in the tensions of the two normotensive eyes (Cases 2 and 6). Case 8 developed acute congestive glaucoma in the right eye one week postoperatively, after a basal iridectomy for the same condition in the left eye. This case was improved by Diamox, which was used prior to the trial on MC-9367. However, the tension rose when Diamox was discontinued.

Table 3 demonstrates the effect of 500 mg. of MC-9367 on 22 eyes of 11 patients with wide-angle glaucoma. Nineteen of these eyes had glaucoma as determined by previous field studies and tonometric readings.

The intraocular pressure of these patients could be controlled only by the combination

of miotics and Diamox. One week prior to the administration of MC-9367 the Diamox was discontinued with consequent rise in tension, as shown in the first column. In Case 5, the right eye showed a reduction of only 3.0 mm. Hg which is considered insignificant. Case 9 also showed insignificant reductions in tension after 500 mg. of Diamox.

Table 4 demonstrates the effect of a single dose of 500 mg. of MC-9367 on the tension of 20 eyes of 10 patients, with 11 eyes showing some form of secondary glaucoma.

Newly discovered cases were started immediately on MC-9367, and after a single dose, Diamox was then instituted for long-range therapy along with any other indicated drugs.

Case 5 was not controlled by miotics alone but was controlled by either Diamox or MC-

TABLE 4
SECONDARY GLAUCOMA

| No. | Age (yr.) | Etiology | Eye | (mm. Hg, Schiøtz) | | | | |
|-----|-----------|--------------------------------|-----|-------------------|---------|-------|-------|-------|
| | | | | Prior | 0.5 hr. | 1 hr. | 2 hr. | 4 hr. |
| 1 | 48 | Aphakic glaucoma | OD | 52 | 35 | 27 | 23 | 23 |
| | | | OS | 23 | 15 | 12 | 11 | 12 |
| 2 | 40 | Uveitis | OD | 55 | 55 | 50 | 40 | 27 |
| | | | OS | 14 | 14 | 15 | 14 | 14 |
| 3 | 66 | Intumes. cataract | OD | 40 | 40 | 40 | 30 | 30 |
| | | | OS | 12 | 14 | 14 | 14 | 14 |
| 4 | 75 | Aphakic glaucoma | OD | 60 | 60 | 55 | 60 | 40 |
| | | | OS | 23 | 23 | 18 | 15 | 12 |
| 5 | 46 | Bilateral disloc. cataract | OD | 40 | — | — | 24 | 20 |
| | | | OS | 40 | — | — | 24 | 20 |
| 6 | 15 | Aphakic glaucoma | OD | 65 | 65 | 40 | 35 | 35 |
| | | | OS | 20 | 20 | 18 | 12 | 12 |
| 7 | 56 | Aphakic glaucoma | OD | 20 | 24 | 24 | 20 | 15 |
| | | | OS | 35 | 35 | 30 | 26 | 20 |
| 8 | 38 | Aphakic glaucoma with rubeosis | OD | 60 | 60 | 60 | 55 | 55 |
| | | | OS | 18 | 15 | 18 | 15 | 14 |
| 9 | 73 | Vascular occlusion glaucoma | OD | 50 | 53 | 52 | 45 | 49 |
| | | | OS | 22 | 20 | 20 | 20 | 20 |
| 10 | 44 | Uveitis | OD | 65 | 65 | 52 | 40 | 26 |
| | | | OS | 20 | 20 | 20 | 18 | 20 |

9367 given with miotics. Case 6 was not controlled by DFP, or by Diamox, when either of these agents was given alone. MC-9367 also failed. The combination of DFP and either Diamox or MC-9367 was effective, however. Case 8, which shows no effective control of tension, was also uncontrolled

after using Diamox with miotic therapy. Case 9 was given a total of 1,500 mg. of MC-9367 in a 24-hour period but the tension still remained elevated.

From these observations it was possible to draw the following conclusions regarding the glaucoma group (table 5):

MC-9367, when combined with the usual miotic drugs, was effective in reducing the intraocular pressure in all 13 eyes with narrow-angle glaucoma. It was effective in 16 out of 19 eyes with wide-angle glaucoma. In the group with secondary glaucoma, it was effective in three out of five cases of aphakic glaucoma, in two cases of glaucoma secondary to uveitis, in two eyes of a patient with glaucoma due to bilateral dislocated cataracts, and in one case of glaucoma due to an intumescent lens. MC-9367 was ineffective in a case of glaucoma due to vascular occlusion, as well as in two cases of aphakic

TABLE 5
SUMMARY

| Condition | No. of Eyes | Effective |
|--|-------------|-----------|
| Narrow-angle glaucoma | 13 | 13 |
| Wide-angle glaucoma | 19 | 16 |
| Aphakic glaucoma | 5 | 3 |
| Glaucoma secondary to uveitis | 2 | 2 |
| Glaucoma secondary to vascular occlusion | 1 | 0 |
| Glaucoma secondary to dislocated lens | 2 | 2 |
| Glaucoma secondary to intumescent cataract | 1 | 1 |
| Control group | 40 | 18 |

glaucoma, one of which was accompanied by rubeosis. In no instance was MC-9367 effective where Diamox had also failed.

SUMMARY AND OBSERVATIONS

1. Squibb MC-9367 in a single dose administered orally is an effective agent in lowering the intraocular pressure in humans.

2. The greatest period of effectivity is two to four hours after administration.

3. The greatest degree of lowering of the intraocular pressure occurred in the eyes of patients with glaucoma.

4. None of the patients reported any paresthesias and no toxic effects were noted after single dosages.

5. The effect of the drug is similar to that seen after a similar dose of Diamox.

CONCLUSION

Squibb MC-9367, a carbonic anhydrase inhibitor, is an effective agent in lowering the intraocular pressure in humans.

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THE RELATION BETWEEN VOGT-KOYANAGI SYNDROME AND SYMPATHETIC OPHTHALMIA*

REPORT OF A CASE OF VOGT-KOYANAGI SYNDROME

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INTRODUCTION

There are three types of uveitis which are accompanied with complicating features in common as their extraocular symptoms, alopecia, poliosis, vitiligo, tinnitus and dysacusia, and dizziness—Vogt-Koyanagi syndrome, Harada's disease, and sympathetic ophthalmia. The similarities among these three conditions have been discussed often, especially in Japan, and recently in America, too, by Cowper,⁵ Bruno and McPherson,³ Swartz,³⁶ and Cordes.⁴ As Cordes mentioned, the weight of current opinion favors the

consideration of Harada's disease and Vogt-Koyanagi syndrome as clinical variants of the same condition, although the relation between them and sympathetic ophthalmia seemed to be more seriously in doubt. There are some authors, especially in Japan, who insist that sympathetic ophthalmia is indeed one of these common diseases.

The greatest difficulty in presuming that sympathetic ophthalmia is a type of Vogt-Koyanagi syndrome or of Harada's disease is, as pointed out by Rados,²⁹ the fact that the former is almost always caused by perforating injuries of one eye. But some cases have been reported in which the disease occurred without injury, or in a person with

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choroidal sarcoma, or with phthisis bulbi. Hamada⁷ and Okamura²⁷ gave, therefore, the opinion that the three diseases were common in nature and sympathetic ophthalmia was only a type of Harada's disease which had a specific history of ocular trauma. Many authors, especially Hamada,⁷ reported in the past on histologic investigations on the problem, but none was of deciding weight because of the poorness of the materials they presented. Recently Ikui, Hiroishi, and Furuyoshi¹¹ reported two cases of Vogt-Koyanagi syndrome, indicating that the histologic picture of this disease was similar to that of sympathetic ophthalmia. Identification of Vogt-Koyanagi syndrome with sympathetic ophthalmia is confused in the evaluation of the role of trauma in sympathetic ophthalmia for the similar uveitis—Vogt-Koyanagi syndrome—occurs without trauma to the eye.

CASE REPORT

On March 25, 1953, H. T., a 72-year-old man, was first seen in the office complaining of loss of vision of the left eye which had begun two days previously. In the summer of 1949, the vision of the right eye had begun to fail with ocular pain and headache; in November, 1949, the right vision was lost entirely. Since then ocular pain occurred occasionally in the right eye. With the left eye there was no pain.

Examination. Right eye. The circumcorneal vessels were dilated and tortuous. The cornea showed irregular opacities scattered through all the surface with superficial vascularization. The pupil was irregularly dilated with no light reflex. There was a small hyphema. The iris had a dusty appearance with some vessels. The lens showed a shimmering brown reflex with pigment spots scattered over the capsule. No structure posterior to the lens could be seen. The ocular tension was 17 mm. Hg (Schiotz). Vision was nil.

Left eye. The eye was slightly injected. The cornea was clear except for a few Descemet wrinkles. The pupil was very small and

distorted, and there were some posterior synechias. There were also fibrin floaters in the anterior chamber. The lens showed cortical opacification and the fundus could not be seen. The tension was 11 mm. Hg (Schiotz). Vision was: 0.1.

Clinical course. He was admitted to our hospital service on March 30, 1953. On March 31st the right eye was enucleated. On April 2nd, lens protein was injected intradermally with the result of a 4.0 by 4.0 mm. area of redness and rigidity. An intradermal injection with the lens material from his enucleated eye revealed no reaction. He complained of headache and of feeling dizzy.

In the following days, the inflammation of the anterior segment of the left eye decreased. Fundus examination revealed a reddish disc with a blurred edge. Later, the inflammation increased both in the anterior and posterior segments. On May 13th many deposits around the pupillary margin could be seen. On May 15th, the Middlebrook-Dubos test of aqueous humor was found to be negative. On May 26th, the protein content of the aqueous humor was 1.8 percent. The deposits on the posterior surface of the cornea increased greatly.

On June 3rd, an intracapsular lens extraction of the left eye was performed without complications, but there was no improvement. On June 20th, alopecia areata of various areas of the scalp was developing and vitiligo was found on the chest and back.

The pupil became more cloudy and by September it was totally occluded with a white membrane.

The treatment from the admission of the patient: subconjunctival injections of cortisone, intravenous injections of Chinophen (Atophan), and systemic administration of aureomycin with atropine locally.

Histologic examination of the enucleated right eye. The lens was taken out for the material of the intradermal sensitivity test. The eye was fixed in formalin and the sections were stained with hematoxylin and eosin.

In the anterior part of the eye there were

dense infiltrations with lymphocytes, plasma cells, and some fibroblasts in the subconjunctival and episcleral tissues. Under the epithelium of the cornea was found a thick connective tissue with vascularizations. The Bowman's membrane beneath the connective tissue was almost intact except some parts where it was ruptured by the tissue. The stroma of the cornea was intact, but in the marginal part there were some invading vessels. There was no wound in the cornea and sclera except the one in the cornea produced at the extraction of the lens after enucleation.

The iris was, in general, thin and atrophic. The root of the iris was adherent to the posterior surface of the cornea, closing the chamber angle completely. At the temporal part of the eye there was a membrane like Descemet's bordering the iris to the anterior chamber, under which and between the anterior layer of the iris an aggregation of plasma cells, lymphocytes, and erythrocytes was seen. At another portion there was a dense layer of infiltrations consisting of cells with large, pale-stained nuclei and with pigment particles over the iris. In the stroma of the iris there were a few lymphocytes. The pigment cells were mostly

shrunk and had lost their projections. In the iris pigment particles were scattered and the vessels were obliterated.

The ciliary body was severely destroyed, the processes were shrunk, and the spaces between them were filled with detached and multiplied unpigmented epithelial cells, cells with large pale-stained nuclei, and lymphocytes. At the nasal side of the ciliary body the suprachoroidal space was widely filled with homogenous pale red-staining substance which extended behind the ora serrata.

The posterior part of the choroid was densely infiltrated with cells, and the anterior part was invaded with a few of them. The choriocapillaris was intact. The infiltrations of the choroid were very diverse. In general there were dense infiltrations with lymphocytes, and of plasma cells with some monocytes and proliferated histiocytes, except in the choriocapillaris. Among the infiltrations were seen here and there, especially in the posterior part, islands of other accumulations of cells, consisting of the so-called epithelioid cells which sometimes enclosed giant cells (figs. 1 and 2). The epithelioid cells with pale-stained large nuclei of an irregular form phagocytized some pigment particles. Near the ora serrata, there



Fig. 1 (Yuge). Infiltration of the choroid, consisting of lymphocytes and plasma cells with a nodule of epithelioid cells in the center. The retina is detached.



Fig. 2 (Yuge). A giant cell in the center of an epithelioid cell nodule.

was formed a dense accumulation of large pigmented and unpigmented cells with lymphocytes elevating the pigment epithelium toward the retina (fig. 3).

The retina was largely detached, especially on the nasal half of the eye. The structure of the retina was almost retained, with a few cell infiltrations in the anterior layer, especially around the vessels. The ganglion

cells were mostly lost and, in the macular region, the retina was edematous, the granular layers being entirely lost. Near the papilla there was a dense layer of glial cells over the retina which extended over the surface of the disc. The pigment epithelium was sometimes broken and its cells were seen isolated from their position in the subretinal space.

The optic nerve was severely infiltrated with chronic inflammatory cells. There was no excavation in the disc; instead there was seen a thick layer of proliferated glial cells.

CASE SUMMARY

The outstanding clinical features of this case are:

1. A mild iritis of the left eye, the right having previously lost all vision perhaps from glaucoma.
2. Slight remission of the iritis of the left eye after enucleation of the right eye with subsequent progression and appearance of deposits on the posterior surface of the cornea.
3. The fundus picture of the left eye with a reddish disc with a blurred edge.
4. Cataract in both eyes and intracapsular

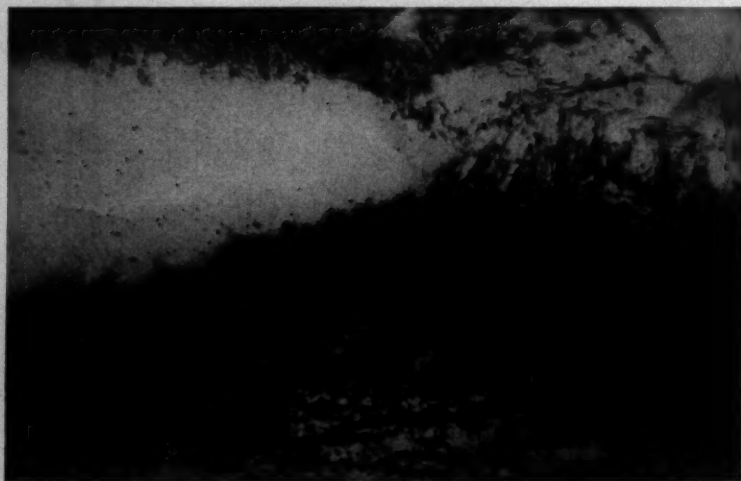


Fig. 3 (Yuge). Elevation of the pigment epithelium near the ora serrata. Accumulation of pigmented and unpigmented large cells and lymphocytes, so-called Dalen-Fuchs nodule.

lens extraction of the left eye without lessening the iritis.

5. Alopecia of an areata type on the head and vitiligo on the chest and back. Also headache and dizziness.

6. Negative Middlebrook-Dubos reaction of the aqueous. X-ray examination of the chest—negative. Skin test with lens protein negative, even with his own lens from the enucleated eye.

DIFFERENTIAL DIAGNOSIS

a. Was the iritis of the left eye excited from the right blind eye?

b. Were both eyes invaded by the toxic or allergic activity of the cataractous lens substance?

c. Were both eye invaded by any other agent from without the eye, the illness of the right eye being a coincidence?

As there was no history of trauma to the right eye and no clinical evidence of such, sympathetic ophthalmia in the ordinary way was not possible. As for the consideration of the lens-induced uveitis, it could be postulated that the iritis of the left eye was a sensitivity reaction to the lens material liberated into the aqueous of the eye, the sensitivity being produced by the right eye. Such a possibility was suggested by Irvine and Irvine,¹³ though it was a case of cataract operation of one eye. Though the cataracts in our case were not of a hypermature type, partial hypermaturity was possible. The enucleation of the right eye was performed for the reason to be discussed later, postulating that the right eye stimulated the iritis of the left eye. But the possible exciting role of the right eye to the disease of the left cannot be excluded because in sympathetic ophthalmia the enucleation of the exciting eye does not always influence the course of the sympathizing eye.

For the reason of the possibility of lens-induced uveitis, the lens of the left eye was extracted intracapsularly but without benefiting the ultimate course of the iritis of the left eye. Thus the toxic or allergic action of

the lens might not have been related in this case.

The histologic picture of the enucleated right eye showed severe infiltrations of the choroid without invading the choriocapillaris. The type of the choroidal infiltrations was a granulomatous one, consisting of many nodular accumulations of epithelioid cells, rarely with giant cells, and without necrosis. Furthermore, there was formed a Dalen-Fuchs' nodule. They are so well known in sympathetic ophthalmia that the repetition of the picture of the disease is not needed.

The cause of the blindness of the right eye might have been glaucoma, the tension already being decreased by the degenerative changes. The edema and loss of cells in the retina of the macular region might be caused by the glaucomatous degeneration of the macula. The optic disc could have been filled with proliferated glial cells after the glaucomatous excavation once occurred.

The detachment of the retina, the edema of the choroid, and the accumulation of serous material in the suprachoroidal space might have been caused by the exudation from the choroidal infiltrations.

DISCUSSION

We feel that there is no doubt that we have here presented a case of uveitis with alopecia and vitiligo, the histologic picture of which resembles that of sympathetic ophthalmia. Whether the case is of Vogt-Koyanagi syndrome or of sympathetic ophthalmia is difficult to determine because the patient had lost the right vision. A case of sympathetic ophthalmia following unoperated glaucoma is not known or not justified and we prefer to consider the case as one of Vogt-Koyanagi syndrome.

That the histologic picture of Vogt-Koyanagi syndrome resembles that of sympathetic ophthalmia in this case is very interesting because the one occurs spontaneously and the other with the special condition in the exciting eye, the role of which is not yet

clarified. If Vogt-Koyanagi syndrome could have been a precipitating factor in one or both eyes, as has been mentioned by Swartz,³⁵ the role of the conditions of sympathetic ophthalmia in the exciting eye might be considered in a different way from those mentioned in the past, postulating that the perforating injury precipitated the occurrence of Vogt-Koyanagi syndrome. This case might be considered as one of sympathetic ophthalmia with degenerative glaucoma as its exciting condition or of Vogt-Koyanagi syndrome with degenerative glaucoma as its precipitating factor.

IDENTITY OF VOGT-KOYANAGI SYNDROME AND HARADA'S DISEASE

Vogt-Koyanagi syndrome and Harada's disease have the following common points:

1. Both are spontaneous, bilateral uveitis with acute onset and chronic, sometimes recurrent course.
2. Both show after recovery a peculiar appearance of the fundi resembling the glow of the evening sky.
3. Both are accompanied by such extra-ocular symptoms as alopecia, poliosis, vitiligo, dizziness, and so forth.

Harada's disease is said to be characteristic in being accompanied with retinal detachment, but this is also observed in Vogt-Koyanagi syndrome, if the fundus can be examined, as reported by Tsuji,⁴⁰ Arisawa,¹ and others. Koh¹⁷ reported that, in his review of nine cases, five had retinal detachments. Rados²⁹ differentiated bilateral uveitis associated with symptoms involving the integument and the hair from bilateral uveitis accompanied by retinal detachment, for the reason that alopecia and poliosis do not figure as integral parts of Harada's disease. But Cowper⁵ stated that the division between the two seemed arbitrary. As has been well discussed by Cordes,⁴ it will be appropriate now to state that the differences between Vogt-Koyanagi syndrome and Harada's disease are not of an absolute nature, but of a relative one; more so, as there are cases

reported indicating the presence of a transitional type between both (Sato,³³ Tsutsui,³⁹ Nakamura,²⁸ Hitomi,¹⁰ and so on.) Takahashi early regarded both diseases as of different types having a common origin, summarizing with the nomenclature "spontaneous, bilateral, severe uveitis."

From the tendency of regarding both diseases as of common origin, the expression "Vogt-Koyanagi type" or "Harada type" of spontaneous uveitis is considered to be most appropriate. Only the difference in prognosis between the two diseases permit the separation, as mentioned by Ishihara.¹⁸ For brevity, I am willing to call the disease Vogt-Koyanagi-Harada syndrome, or in a more general sense, oculo-oto-cutaneous syndrome.

Rubino³² called Harada's disease "uveo-meningitisches Syndrom," and Cowper, identifying Vogt-Koyanagi syndrome and Harada's disease, "uveo-encephalitis," to which Remky³¹ agreed.

RELATION BETWEEN VOGT-KOYANAGI-HARADA SYNDROME AND SYMPATHETIC OPHTHALMIA

Koyanagi¹⁸⁻¹⁹ and Harada⁸ pointed out their similarity. As many subsequent reports show, sympathetic ophthalmia sometimes is like Vogt-Koyanagi syndrome, sometimes like Harada's disease. Parker²⁸ stated that Vogt-Koyanagi syndrome resembled a case of bilateral sympathetic ophthalmia. The only difference is that sympathetic ophthalmia occurs after ocular perforating injury, while Vogt-Koyanagi-Harada syndrome occurs spontaneously.

The similarity of Vogt-Koyanagi-Harada syndrome and sympathetic ophthalmia is not only in their clinical appearance but also in their histologic features. Though, earlier, Kitazawa¹⁶ and, later, Ogawa²⁶ Sugimoto and Kodama³⁵ argued against their histologic similarity, Matsuoka²¹ and others have insisted that their histologic features are the same. The discrepancy was considered to be in that the materials used by Kitazawa,¹⁶ Ogawa,²⁶ Sugimoto and Kodama were of the

later stage of Vogt-Koyanagi-Harada syndrome. Recently Ikui, Hiroishi, and Furuyoshi¹¹ reported two cases of Vogt-Koyanagi syndrome with detailed histologic investigations, concluding that the similarity of sympathetic ophthalmia and Vogt-Koyanagi syndrome in the histologic features was certain, referring to their previously undertaken review of many cases of sympathetic ophthalmia. In these reports they presented the opinion that the so-called epithelioid cells of sympathetic ophthalmia and Vogt-Koyanagi syndrome were derived from proliferation of pigment cells of the uvea, caused perhaps by a special virus. This postulation was founded on the demonstration of the dopa-oxidase and silver reaction in the epithelioid cells.

Swartz²⁶ obtained a piece of iris at the time of iridencleisis in his case and declared that he felt it was safe to assume that the pathologic findings in the nontrauma-precipitated Vogt-Koyanagi syndrome and the trauma-precipitated sympathetic ophthalmia were certainly similar enough to make differentiation quite difficult.

The histologic picture of the presented case resembles that of sympathetic ophthalmia. The materials used by Matsuoka,²¹ Okamura,²⁷ Isajiki,¹⁴ and Swartz, leading to the conception of the resemblance of Vogt-Koyanagi syndrome and sympathetic ophthalmia, were insufficient to verify it, because they were pieces of iris. In the case presented by Hamada,⁷ who most strongly insisted on the similarity between the diseases, there were two cases of Harada's disease involved which occurred with phthisis in one or both eyes. Objections were raised against the fact that he regarded the cases of sympathetic ophthalmia with phthisis purposely as of Harada's disease. In the cases of Ikui, Hiroishi, and Furuyoshi¹¹ and my case, whole eyeballs were used and so the conclusion that both diseases resembled each other in their histologic pictures should be more satisfactory.

Concerning the role of precipitating factor

in Vogt-Koyanagi-Harada syndrome and of exciting injury in sympathetic ophthalmia:

It is a well-known fact that sympathetic ophthalmia occurs after a perforating injury in one of the eyes and that when the injured eye is enucleated it does not occur. But there were cases reported in which sympathetic ophthalmia occurred with choroidal sarcoma, after contusion or subconjunctival scleral rupture; in a word, without a perforating injury. Even in connection with trauma, some cases of sympathetic ophthalmia were reported occurring in 10 or 20 years after the occasion or in some with phthisis or staphyloma corneae. Schreck²⁴ mentioned these cases as of "Spätfektion."

In the face of typical cases we cannot but summarize the diseases as follows:

1. Sympathetic ophthalmia is a bilateral, severe uveitis excited by a perforating injury on one of the eyes.

2. Vogt-Koyanagi-Harada syndrome is a bilateral severe uveitis with spontaneous onset.

Then, how should those cases of sympathetic ophthalmia occurring long after the trauma or without perforating injuries in one of the eyes and those of Vogt-Koyanagi-Harada syndrome occurring with precipitating factors in one of the eyes be treated?

Hamada⁷ stated that sympathetic ophthalmia was Harada's disease with trauma to one eye. Nakamura²⁵ believes that Harada's disease is spontaneous sympathetic ophthalmia without trauma.

Swartz²⁶ considered his case to be Vogt-Koyanagi syndrome precipitated by lens extraction. If ocular surgery can be considered a precipitating factor of Vogt-Koyanagi-Harada syndrome, it is easy to find many cases in those of sympathetic ophthalmia. Tamura²⁸ reported a case of Harada's disease which occurred after a small iris prolapse healed and many cases of sympathetic ophthalmia have been reported in which the perforating injuries in the exciting eyes were slight and small, though with prolapses

of the iris. In identifying Vogt-Koyanagi-Harada syndrome as sympathetic ophthalmia we must not be confused in evaluating the roles of precipitating factors of the former or the exciting injuries of the latter.

The prophylactic effects of enucleation should, however, be considered because, if the injured eye is enucleated soon after the trauma, the disease does not occur. The ocular injury, which has such a role in the case of sympathetic ophthalmia, cannot be regarded as a precipitating factor in Vogt-Koyanagi-Harada syndrome which usually occurs spontaneously and may occur even after the eye has been enucleated after the onset of the injury. In the case report of this paper, the disease of the right eye should be regarded as a coincidence, though it seems to have precipitated the disease.

The ocular injury, therefore, is the indispensable factor in the causation of sympathetic ophthalmia; in other words, sympathetic ophthalmia is an "eye-conditioned oculo-oto-cutaneous syndrome," while Vogt-Koyanagi-Harada syndrome is a seemingly non-conditioned one. Then it is easy to consider that choroidal sarcoma or phthisis bulbi are also factors in the occurrence of eye-conditioned oculo-oto-cutaneous syndrome, in the sense that we can willingly avoid the onset of the disease by preventive enucleation. It is not yet known whether Vogt-Koyanagi-Harada syndrome is really unconditioned or seemingly unconditioned, or merely noneye-conditioned.

As for the origins of Vogt-Koyanagi-Harada syndrome and of sympathetic ophthalmia, many authors suggest the presence of specific viruses. The virus, if such exists in the case of sympathetic ophthalmia, need not always multiply in the whole uvea to produce the characteristic granulomatous inflammation, for the observation of Redslob³⁰ suggests that the agent can enter the body after it has set up a scaffolding in the form of chancre d'inoculation, to which Ikui et al.¹¹ agreed. In the Vogt-Koyanagi-Harada syndrome the virus would be able to enter

from anywhere in the body and then propagate and invade all the pigmented organs in the body. The essential of oculo-oto-cutaneous syndrome is the affection of pigment cells in the whole body. Even the dysacusia can be ascribed to the affection of the pigment tissue in the labyrinth. (The presence of pigments in the labyrinth is described in many books, though it was denied by Parker²⁸ and Cowper⁵ in the basilar membrane.)

Lerner and Fitzpatrick²⁰ described: "Under ordinary conditions melanocytes probably multiply at a slow rate. This belief seems tenable, because, when these cells are destroyed by physical or chemical means, permanent depigmentation results." Alopecia, vitiligo, and dysacusia may be caused by the destruction of the pigment cells. It is to be noted that the essential feature of the uveitis in Vogt-Koyanagi-Harada syndrome and sympathetic ophthalmia is the destruction of the pigment cells in the tissue. In my histologic examination of the skin in another case of Vogt-Koyanagi-Harada syndrome proliferation of connective tissue cells in the depigmented area was revealed.

Melanocytes are found in the skin, eyes, and central nervous system. It is not impossible, therefore, to postulate a chancre d'inoculation in the brain in the case of Vogt-Koyanagi-Harada syndrome, as seen in the eye in the case of sympathetic ophthalmia, a consideration similar to that of Swartz. Then some factors might play a role in establishing uveitis in the eye as the precipitating factor. But these factors cannot be paralleled with the perforating injuries of the eye in the case of sympathetic ophthalmia, because the latter are factors permitting the virus, if such exists, to enter the body.

So far as is mentioned, several factors precipitating the causation of Vogt-Koyanagi-Harada syndrome can be postulated, such as scratching a pigmented region of skin (Tsutsui³⁹), overaction in general or of the eye (Yoshida,⁴² Hamada,⁷ Minami⁴²), trauma of eye region or forehead (Tsut-

sui¹⁹), pregnancy (Koh¹⁷). These preceded the occurrence of the disease in their cases.

Vogt-Koyanagi-Harada syndrome and sympathetic ophthalmia are sometimes susceptible to cortisone, antibiotics, and the sulfa compounds. Asayama, Hirotani, and Yamada² reported therapeutic improvement in cases of Vogt-Koyanagi-Harada syndrome with sulfamerazine. Improvement with Chloromycetin has been reported in Vogt-Koyanagi-Harada syndrome by Mikuni and Matsumoto²² and others, and in sympathetic ophthalmia by Mikuni and Yoneyama.²³ Many favorable reports have been published on the effect of cortisone, such as those of Ikui and Furuyoshi,¹² Yamamoto,⁴¹ Haik and Waugh, Jr.,⁶ and others. An infectious cause seems more likely than one of pigment allergy. However, Lerner and Fitzpatrick have suggested that radioactively labeled antityrosinase might be able to localize in and destroy melanocytes (Knorpp). The selec-

tive invasion of pigment cells in the body is therefore not impossible.

SUMMARY

1. A case of Vogt-Koyanagi syndrome, in which the vision of one eye had been lost previously from glaucoma, is presented.

2. Histologic investigation of the enucleated glaucomatous eye showed the typical features of sympathetic ophthalmia.

3. The role of an exciting factor in sympathetic ophthalmia and of a precipitating factor in Vogt-Koyanagi syndrome is discussed.

4. The three conditions, Vogt-Koyanagi syndrome, Harada's disease, and sympathetic ophthalmia, were identified, the former two were summarized as Vogt-Koyanagi-Harada syndrome and all three as oculo-otocutaneous syndrome.

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THE USE OF CHLORPROMAZINE IN CATARACT SURGERY*

A PRELIMINARY REPORT

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Nausea and vomiting during the operative or postoperative period in intraocular surgery are symptoms which have caused considerable concern to the ophthalmic surgeon. These symptoms may lead to serious sequelae and any drug or method which might reduce these complications should be most helpful. Furthermore, in ophthalmic surgery in which operations are frequently per-

formed under local anesthesia, there has been a need for an effective adjuvant to tranquilize the patient. Chlorpromazine was chosen for this study because of its reputed ability to relieve anxiety and reduce the incidence of nausea and vomiting.

An attempt has been made to evaluate the usefulness of chlorpromazine (Thorazine®) in 100 consecutive cataract extractions. The results have been compared with a previous series of 100 consecutive cataract extractions in which chlorpromazine was not used.

Chlorpromazine is relatively new in this

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country and as Williams has so aptly expressed in the *Journal of the American Medical Association* (September 11, 1954): "The early history of a dramatic new drug frequently falls into a pattern which we have learned to recognize. Upon introduction it meets with wary skepticism. Soon it is carried on a wave of enthusiasm to a peak of acceptance and it becomes enthusiastically proclaimed beyond what seemed reasonable, then, with the inevitable reports of limitations and unwanted side-reactions, which are frequently distorted by uncritical talk and rumor, the drug falls sharply into disfavor. Finally, it climbs back again to its true level among the large group of useful drugs."

One of the primary purposes of this report is to study the actual value of chlorpromazine during the current wave of enthusiasm for this drug. We have attempted to judge the status of the drug insofar as is possible on the basis of clinical trial. Reports in the ophthalmic literature have not been numerous to date.

HISTORICAL DATA

Chlorpromazine was first used by French investigators for surgical cases in 1951. Subsequently, the clinical application of chlorpromazine was studied elsewhere on the Continent and in Great Britain. The drug was introduced to the United States in May, 1954. In the brief period of two years it is estimated that it has been administered to over seven million patients. A rapidly growing bibliography on this drug indicates that it has usefulness in the treatment of nausea and vomiting, mental and emotional disturbances, alcoholism, intractable pain, protracted hiccoughs, obstetrics, asthma, neurodermatitis, and in drug addiction for symptoms after withdrawal.

It would appear to be a valuable drug for pre- and postoperative medication in ocular surgery. Becker¹ reported first in the ophthalmic literature of this country that the therapeutic administration of Thorazine® to adults in doses of 50 mg. intramuscularly and

25 mg. orally every four to six hours alleviated dramatically all instances of nausea and vomiting following surgery on the eye.

Hanno,² however, warned against the indiscriminate use of chlorpromazine on a routine basis until the drug has had a more critical evaluation. He refers to the complication of intrahepatic biliary obstruction and one death with jaundice reported in the English literature. According to Hanno, vomiting is a rare postoperative complication at the Wills Eye Hospital because of attention to these factors: (1) Use of Demerol and barbituates rather than morphine, (2) local anesthesia rather than general, and (3) early attention to postoperative abdominal distention.

PHARMACOLOGY

Chlorpromazine which chemically is 10-(3-dimethylaminopropyl)-2-chlorphenothiazine has a varied pharmacologic effect. According to Nutt and Wilson,³ it is capable of initiating: (1) Production of sleep as a tranquilizer and general lowering of the metabolic rate, (2) potentiation of the action of other analgesics and anesthetic drugs, (3) depressant effect on the vomiting centers, and (4) some reduction in muscular tone and a probable anti-adrenalin effect. It is believed that chlorpromazine acts principally on higher neural centers in the general area of the diencephalon, selectively inhibiting the chemoreceptor trigger zone, the hypothalamus, and the reticular substance.⁴ These centers are believed to control vomiting, heat regulation, wakefulness, vasomotor, and muscle tone.

PREVIOUS REPORTS

It has been estimated that there have been over 4,500 reports on chlorpromazine in the medical literature throughout the world. Many of the articles stress the antiemetic and tranquilizing qualities of the drug but there has been a relative paucity of material dealing with ophthalmic surgery. Nutt and Wilson⁵ describe their experiences with 80 surgical cases including cataract extraction, glau-

TABLE 1
PRE-THORAZINE

| No. | Name | Age (yr.) | Nausea | Vomiting | Medical Complications | Remarks |
|-----|-------|-----------|--------|----------|-----------------------|---|
| 1 | A. C. | 67 | 0 | 0 | 0 | Chronic glaucoma |
| 2 | A. A. | 75 | 0 | 0 | 0 | |
| 3 | M. B. | 64 | 0 | 0 | 0 | |
| 4 | R. P. | 81 | 0 | 0 | 0 | |
| 5 | L. M. | 75 | 0 | 0 | 0 | |
| 6 | I. M. | 83 | 0 | 0 | 0 | |
| 7 | W. F. | 48 | 0 | 0 | 0 | |
| 8 | M. H. | 70 | 0 | 0 | 0 | |
| 9 | E. B. | 60 | 0 | 0 | 0 | |
| 10 | M. J. | 66 | 0 | 0 | 0 | |
| 11 | L. G. | 60 | 1+ | 0 | 0 | |
| 12 | E. H. | 42 | 0 | 0 | 0 | |
| 13 | A. S. | 62 | 0 | 0 | 0 | |
| 14 | E. P. | 72 | 0 | 0 | 0 | |
| 15 | Y. L. | 62 | 2+ | 0 | 0 | |
| 16 | E. C. | 70 | 0 | 0 | 0 | |
| 17 | M. C. | 74 | 3+ | 3+ | 0 | |
| 18 | F. G. | 57 | 0 | 0 | Diabetes | |
| 19 | M. S. | 49 | 0 | 0 | 0 | |
| 20 | D. D. | 49 | 0 | 0 | 0 | Severe apprehension |
| 21 | D. G. | 80 | 0 | 0 | 0 | |
| 22 | O. T. | 73 | 1+ | 1+ | 0 | |
| 23 | M. E. | 65 | 2+ | 0 | 0 | |
| 24 | J. M. | 62 | 0 | 0 | 0 | |
| 25 | P. N. | 65 | 0 | 0 | 0 | |
| 26 | E. J. | 54 | 0 | 0 | 0 | |
| 27 | R. B. | 70 | 0 | 0 | 0 | |
| 28 | G. R. | 68 | 1+ | 1+ | 0 | |
| 29 | J. R. | 78 | 0 | 0 | 0 | |
| 30 | M. R. | 71 | 1+ | 0 | 0 | |
| 31 | F. C. | 67 | 4+ | 4+ | 0 | |
| 32 | L. V. | 69 | 4+ | 4+ | 0 | |
| 33 | A. M. | 69 | 0 | 0 | 0 | |
| 34 | H. B. | 62 | 0 | 0 | 0 | |
| 35 | E. C. | 72 | 1+ | 1+ | 0 | |
| 36 | D. D. | 52 | 2+ | 2+ | 0 | |
| 37 | A. F. | 57 | 4+ | 4+ | 0 | |
| 38 | D. C. | 66 | 3+ | 0 | 0 | |
| 39 | J. G. | 71 | 0 | 0 | 0 | Severe apprehension— paraldehyde given |
| 40 | H. F. | 82 | 0 | 0 | 0 | |
| 41 | M. C. | 68 | 4+ | 1+ | 0 | Confused |
| 42 | A. L. | 58 | 2+ | 1+ | 0 | |
| 43 | A. C. | 63 | 1+ | 0 | 0 | Chronic glaucoma |
| 44 | W. P. | 54 | 1+ | 1+ | 0 | |
| 45 | R. H. | 77 | 2+ | 2+ | 0 | |
| 46 | E. H. | 53 | 0 | 0 | 0 | |
| 47 | H. R. | 58 | 0 | 0 | 0 | |
| 48 | M. F. | 53 | 0 | 0 | 0 | |
| 49 | J. L. | 78 | 0 | 0 | 0 | |
| 50 | R. G. | 69 | 0 | 0 | 0 | |
| 51 | A. B. | 54 | 0 | 0 | 0 | |
| 52 | M. V. | 70 | 0 | 0 | 0 | |
| 53 | T. R. | 70 | 0 | 0 | 0 | |
| 54 | P. N. | 66 | 0 | 0 | 0 | |
| 55 | E. B. | 58 | 2+ | 1+ | 0 | |
| 56 | W. L. | 65 | 0 | 0 | 0 | |
| 57 | C. H. | 66 | 0 | 0 | 0 | |
| 58 | F. W. | 73 | 0 | 0 | 0 | |
| 59 | G. W. | 65 | 0 | 0 | 0 | Iritis, boiled milk given |
| 60 | E. B. | 70 | 0 | 0 | 0 | |
| 61 | A. T. | 70 | 0 | 0 | 0 | |
| 62 | M. N. | 76 | 4+ | 4+ | 0 | |
| 63 | T. C. | 81 | 3+ | 2+ | 0 | |
| 64 | J. K. | 63 | 0 | 0 | Diabetes | |
| 65 | E. E. | 78 | 3+ | 3+ | 0 | |

TABLE 1—(continued)

| No. | Name | Age (yr.) | Nausea | Vomiting | Medical Complications | Remarks |
|-----|-------|-----------|--------|----------|------------------------|------------------------------------|
| 66 | W. F. | 49 | 0 | 0 | 0 | |
| 67 | C. B. | 54 | 0 | 0 | 0 | |
| 68 | M. B. | 75 | 0 | 0 | Diabetes | |
| 69 | F. A. | 69 | 0 | 0 | 0 | |
| 70 | J. A. | 70 | 0 | 0 | 0 | |
| 71 | J. S. | 69 | 0 | 0 | 0 | Chronic glaucoma |
| 72 | C. T. | 73 | 0 | 0 | Diabetes | |
| 73 | H. W. | 68 | 0 | 0 | 0 | |
| 74 | M. S. | 50 | 1+ | 0 | 0 | |
| 75 | F. W. | 64 | 0 | 0 | 0 | Iritis, boiled milk |
| 76 | S. S. | 55 | 0 | 0 | 0 | |
| 77 | D. E. | 52 | 0 | 0 | Diabetes | |
| 78 | E. L. | 70 | 0 | 0 | 0 | Confused and anxious |
| 79 | M. N. | 75 | 0 | 0 | 0 | |
| 80 | R. G. | 77 | 0 | 0 | Chronic Bronchiectasis | |
| 81 | M. H. | 3 | 0 | 0 | 0 | Confused |
| 82 | O. F. | 74 | 0 | 0 | 0 | |
| 83 | L. M. | 85 | 0 | 0 | 0 | |
| 84 | M. C. | 68 | 0 | 0 | 0 | |
| 85 | J. T. | 80 | 0 | 0 | 0 | |
| 86 | C. M. | 62 | 0 | 0 | 0 | Retinitis pigmentosa |
| 87 | R. E. | 59 | 0 | 0 | 0 | Chronic Glaucoma |
| 88 | L. S. | 60 | 0 | 0 | 0 | |
| 89 | E. C. | 74 | 0 | 0 | 0 | |
| 90 | A. C. | 65 | 1+ | 0 | 0 | |
| 91 | E. B. | 61 | 4+ | 4+ | 0 | |
| 92 | N. R. | 69 | 4+ | 4+ | 0 | |
| 93 | I. E. | 52 | 0 | 0 | Diabetes | |
| 94 | L. E. | 69 | 0 | 0 | 0 | Chronic glaucoma |
| 95 | M. S. | 74 | 0 | 0 | 0 | Confused |
| 96 | A. P. | 76 | 0 | 0 | 0 | |
| 97 | H. C. | 66 | 0 | 0 | 0 | |
| 98 | F. E. | 86 | 0 | 0 | Cardiac | Confused nausea on 4th postop. day |
| 99 | H. I. | 69 | 0 | 0 | 0 | |
| 100 | L. G. | 76 | 1+ | 0 | 0 | Confused |

coma, and corneal grafting operations. They stress the chief advantages as (1) no co-operation is required from the patient during surgery or immediately postoperatively, (2) it produces a low tension eye ideal for surgery, and (3) the recovery period is extremely tranquil.

Moore⁶ discussed a series of 58 eye surgical patients who received chlorpromazine as premedication and stated that "barbituates given alone may make a patient drowsy to the point of sleeping but do not diminish the fear of and reaction to the pain produced by the necessary injections, nor do they allay preoperative anxiety." He found, however, that "the patient's nervousness may be lessened" by the oral use of this drug and thought that chlorpromazine (Largactil) pro-

duced a calmer, more relaxed, and co-operative patient.

The use of chlorpromazine in ocular surgery in 22 psychotic and 23 nonpsychotic patients who have undergone major ocular surgery has been studied and reported by Byerly, Murray, Winter, and Vitols.⁷ Preoperatively chlorpromazine was found to calm and relax the patient, reduce anxiety and apprehension and lessen the amount of sedation and analgesia required. During surgery the drug reduced restlessness, controlled vomiting, and enhanced anesthesia. Postoperatively, in conjunction with small doses of analgesics or sedatives, it relieved pain and controlled nausea, vomiting, hiccoughs, and confusion.

The experience of Burn, Hopkin, Ed-

wards, and Jones⁸ in Great Britain has been similar. In 89 patients under local anesthesia a combination of chlorpromazine, promethazine and pethidine gave unquestionable improvement as noted by the absence of apprehension or tenseness, greater muscular relaxation, and minimal bleeding. The authors were impressed by the advantage over barbituate sedation alone.

Following general anesthesia, it has been estimated by Albert and Coakley⁹ that nearly 25 percent of the patients develop distressing postanesthetic vomiting. These authors report that the oral administration of 50 mg. of chlorpromazine preoperatively reduced the incidence of vomiting after general anesthesia by 50 percent.

Fritz¹⁰ reports on the use of chlorpromazine in 25 cases under local anesthesia involving the eye, nose, and throat. There was no nausea, vomiting, or anxiety. Somnolence was pronounced and amnesia noted frequently. No complications attributed to the drug were noted. Paul and Leopold¹¹ found that systemically administered chlorpromazine lowered intraocular pressure in experimental animals. This adds support to a similar observation on the human eye and indicates a probable side advantage of this drug for intraocular surgery.

MATERIAL, DOSAGE, AND TECHNIQUE

The first 100 consecutive cataract extractions had the following preoperative routine: sodium pentobarbital (Nembutal®) 100 mg. the evening preceding surgery, nothing by mouth four hours preoperatively, sodium pentobarbital 100 mg. four hours preoperatively, and sodium pentobarbital 100 mg. one hour preoperatively, meperidine (Demerol) 50 to 100 mg. according to weight and age, and demenhydrinate (Dramamine) 50 mg. one half hour preoperatively. Postoperatively: meperidine 50 mg. every four hours, as required for pain, or aspirin 600 mg. was prescribed.

The second 100 consecutive cataract extractions had the identical preoperative orders

with the addition of chlorpromazine 25 mg. orally one half hour preoperatively. Chlorpromazine 25 mg. was given parenterally immediately postoperatively and again every three hours for nausea or vomiting as required.

The control series of 100 cataract extractions and the chlorpromazine series of 100 cases were subjected to the identical technique in each instance. The procedure included the preparation of a limbal-based flap and two preplaced grooved 6-0 chromic gut sutures. Delivery of the lens was accomplished with an erisophake or a capsule forceps. Intracapsular extractions were attempted in all cases and were successful in 83 percent of the first series and 95 percent in the second 100 cases. All cases were done under local anesthesia using two-percent procaine for akinesia by the O'Brien and Atkinson method and a retrobulbar block.

It has been found that the optimum time for surgery occurs between one-half hour to two hours following the premedication. The clinical effects of chlorpromazine appear to last for four to eight hours.

RESULTS

The quantitative and qualitative measurement of tranquility and the degree of anxiety with or without chlorpromazine does not lend itself easily to calibration and one must rely on clinical judgment.

A careful review of the 100 cataract operations performed prior to chlorpromazine discloses that 80 percent of the patients were judged to be reasonably co-operative during the operation and without evidence of marked anxiety during the postoperative period. These patients received the usual routine pre- and postoperative medication with the exception of chlorpromazine. However, in the 100 cataract cases in which chlorpromazine was used, it was judged that 91 percent of the patients were completely relieved of preoperative tension and continued through the postoperative phase in a calm and detached manner. Nine patients

came to the operating room as wide awake and apprehensive as though no premedication had been given. Patients who were particularly apprehensive were more inclined to be nauseated and vomit postoperatively.

One may conclude that there is at least a 10-percent improvement in tranquility during the operative and immediate postoperative phase for those patients receiving chlorpromazine. This is not a statistically significant figure. The tranquilizing and calming effect of chlorpromazine has an impressive therapeutic effect on apprehensive, tense, and anxious patients. This unique quality of the drug is of tremendous value to the surgeon and patient alike in the operating room and during the immediate postoperative period. This fact does not reveal itself in figures but only by clinical observation.

Twenty-one of the patients had their first cataract operation in the first series and their second cataract operation for the second eye in the chlorpromazine series. They were nearly unanimous in their comment that it was less distressing the second time in comparison with the first operation. Prior to the

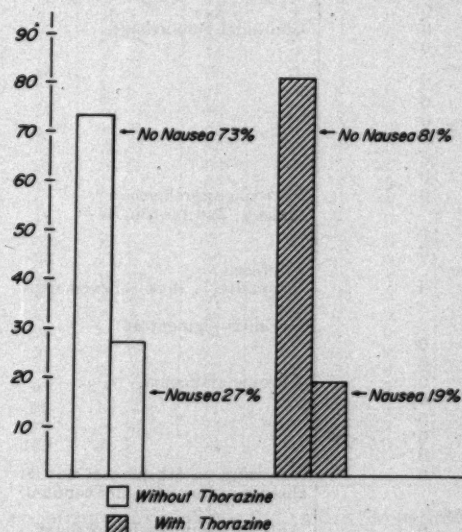


Fig. 1 (Harley and Mishler). Incidence of nausea with and without Thorazine in 200 consecutive cataract extractions.

| | Minimal Nausea | Severe Nausea | Total |
|----------------------|----------------|---------------|-------|
| No Thorazine Control | 16 | 11 | 27 |
| Thorazine | 16 | 3 | 19 |

Fig. 2 (Harley and Mishler). Frequency of nausea in 200 cataract extractions

use of chlorpromazine one frequently heard that the cataract operation on the second eye was much more uncomfortable.

The act of vomiting allows one to be much more objective about recording figures. Since this emesis is almost invariably accompanied by nausea, there is a certain reduplication of figures. Nurses and attendants were particularly attentive to the symptom of nausea as a precursor of vomiting. When nausea occurred, one could give chlorpromazine and frequently prevent emesis. Nausea and vomiting were further subdivided into minimal and severe. Minimal nausea or vomiting occurred once or twice while the severe form occurred three times or more. It becomes evident that severe vomiting is of primary concern and the major symptom to be watched for and reduced to a minimum (figs. 1, 2, 3, and 4).

Statistical analysis of these results indicates that the number of cases is sufficiently large (100 cases without chlorpromazine and 100 cases with chlorpromazine) to reach or exceed the five-percent level of probability for a chi-squared test of the double dichotomy.

Minimal nausea was identical in number in both series. Chlorpromazine seemed to have little effect on minimal nausea in our series. It appears most useful in severe nausea and vomiting. There seems to be a high degree of correlation between anxiety and apprehension and minimal nausea. There were no cases of emesis during surgery. One patient had emesis preoperatively but was controlled with chlorpromazine.

In our series abdominal distention was

TABLE 2
POST-THORAZINE

| No. | Name | Age (yr.) | Nausea | Vomiting | Medical Complications | Remarks |
|-----|-------|-----------|--------|----------|--|---|
| 1 | M. M. | 72 | 0 | 0 | Anemia | |
| 2 | H. K. | 50 | 0 | 0 | Hypertension | |
| 3 | B. R. | 49 | 4+ | 4+ | 0 | Severe anxiety, required sedation |
| 4 | H. D. | 75 | 0 | 0 | 0 | |
| 5 | R. K. | 71 | 0 | 0 | 0 | |
| 6 | J. K. | 55 | 0 | 0 | 0 | |
| 7 | G. S. | 79 | 0 | 0 | 0 | |
| 8 | T. S. | 77 | 0 | 0 | Arteriosclerotic heart disease | Required digitalis |
| 9 | J. B. | 73 | 0 | 0 | 0 | |
| 10 | N. R. | 82 | 0 | 0 | Headaches | |
| 11 | J. S. | 62 | 0 | 0 | Hypertension Hypertension Paroxysmal tachycardia | |
| 12 | W. B. | 66 | 0 | 0 | 0 | Secondary glaucoma-boiled milk, 10 cc. |
| 13 | D. P. | 41 | 0 | 0 | 0 | |
| 14 | A. S. | 65 | 1+ | 1+ | 4th postop. day Pulmonary infarct | |
| 15 | M. C. | 79 | 4+ | 4+ | Distended bladder 2nd postop. day Enema and catheterization relieved symptoms | |
| 16 | L. E. | 79 | 0 | 0 | 0 | |
| 17 | A. B. | 67 | 0 | 0 | 9 | |
| 18 | J. I. | 70 | 2+ | 1+ | Coronary infarction 1st postop. day | |
| 19 | S. L. | 56 | 0 | 0 | 0 | |
| 20 | M. T. | 60 | 1+ | 0 | 0 | |
| 21 | W. F. | 62 | 0 | 0 | 0 | |
| 22 | M. M. | 58 | 0 | 0 | 0 | |
| 23 | E. E. | 70 | 0 | 0 | 0 | Choroidal hemorrhage |
| 24 | M. C. | 65 | 0 | 0 | 0 | |
| 25 | H. L. | 62 | 0 | 0 | Diabetes | |
| 26 | A. B. | 58 | 1+ | 0 | 0 | |
| 27 | G. J. | 54 | 0 | 0 | 0 | |
| 28 | E. J. | 60 | 0 | 0 | 0 | |
| 29 | C. L. | 64 | 2+ | 0 | 0 | |
| 30 | M. S. | 61 | 0 | 0 | 0 | |
| 31 | M. M. | 63 | 0 | 0 | 0 | |
| 32 | E. C. | 59 | 2+ | 0 | 0 | Extreme apprehension Nausea, 2nd postop. day |
| 33 | A. M. | 49 | 0 | 0 | 0 | |
| 34 | L. S. | 64 | 0 | 0 | 0 | |
| 35 | A. T. | 66 | 0 | 0 | Cardiac | Confused |
| 36 | A. M. | 70 | 1+ | 0 | 0 | Thorazine, 1 dose relieved nausea Retinitis pigmentosa |
| 37 | D. M. | 65 | 0 | 0 | 0 | |
| 38 | A. Z. | 70 | 0 | 0 | 0 | |
| 39 | C. B. | 58 | 0 | 0 | 0 | Chronic glaucoma |
| 40 | B. C. | 72 | 0 | 0 | 0 | |
| 41 | A. M. | 73 | 0 | 0 | 0 | |
| 42 | S. M. | 75 | 0 | 0 | 0 | |
| 43 | D. C. | 70 | 0 | 0 | 0 | |
| 44 | C. A. | 65 | 2+ | 2+ | 0 | Vomiting on 5th postop. day in absence of thorazine, not counted. |
| 45 | M. P. | 66 | 0 | 0 | Diabetes | |
| 46 | J. C. | 51 | 0 | 0 | 0 | Anterior chamber hemorrhage. |
| 47 | S. S. | 74 | 4+ | 2+ | 0 | Vomiting on 3rd postop. day in absence of thorazine, not counted |
| 48 | M. S. | 66 | 0 | 0 | 0 | |

TABLE 2—continued

POST-THORAZINE

| No. | Name | Age (yr.) | Nausea | Vomiting | Medical Complications | Remarks |
|-----|-------|-----------|--------|----------|-----------------------|---|
| 49 | W. F. | 58 | 0 | 0 | 0 | |
| 50 | D. S. | 73 | 0 | 0 | 0 | |
| 51 | L. M. | 70 | 0 | 0 | 0 | |
| 52 | S. L. | 48 | 0 | 0 | 0 | |
| 53 | H. C. | 67 | 0 | 0 | 0 | |
| 54 | M. G. | 67 | 0 | 0 | 0 | |
| 55 | A. T. | 67 | 1+ | 1+ | 0 | Uveitis, activated boiled milk 10 cc., one-eyed patient, apprehensive |
| 56 | E. W. | 70 | 0 | 0 | 0 | |
| 57 | M. C. | 43 | 0 | 0 | 0 | |
| 58 | C. M. | 76 | 3+ | 2+ | | Typhoid fever therapy, uveitis activated. Nausea & vomiting on 5th postop. day, in absence of Thorazine not counted |
| 59 | L. S. | 82 | 0 | 0 | 0 | |
| 60 | M. S. | 76 | 0 | 0 | 0 | |
| 61 | R. G. | 70 | 0 | 0 | 0 | |
| 62 | G. W. | 70 | 0 | 0 | 0 | |
| 63 | J. K. | 60 | 0 | 0 | 0 | |
| 64 | G. K. | 60 | 0 | 0 | 0 | |
| 65 | E. D. | 60 | 2+ | 1+ | 0 | |
| 66 | C. H. | 67 | 1+ | 0 | Cardiac | |
| 67 | S. N. | 58 | 0 | 0 | 0 | |
| 68 | A. L. | 59 | 0 | 0 | 0 | |
| 69 | A. C. | 65 | 1+ | 0 | 0 | |
| 70 | I. F. | 75 | 0 | 0 | 0 | |
| 71 | M. R. | 54 | 0 | 0 | Diabetes | |
| 72 | L. N. | 73 | 0 | 0 | 0 | |
| 73 | J. S. | 53 | 4+ | 3+ | 0 | |
| 74 | M. F. | 75 | 0 | 0 | 0 | Confused |
| 75 | G. S. | 59 | 2+ | 1+ | 0 | Anterior chamber hemorrhage |
| 76 | M. N. | 78 | 0 | 0 | 0 | |
| 77 | H. L. | 69 | 1+ | 0 | 0 | 1 dose thorazine stopped nausea |
| 78 | P. K. | 45 | 0 | 0 | 0 | |
| 79 | T. S. | 76 | 0 | 0 | 0 | |
| 80 | J. M. | 60 | 0 | 0 | 0 | |
| 81 | R. S. | 48 | 0 | 0 | 0 | Intraocular hemorrhage |
| 82 | R. A. | 50 | 0 | 0 | 0 | |
| 83 | H. B. | 53 | 0 | 0 | Cardiac diabetes | |
| 84 | A. S. | 50 | 0 | 0 | 0 | |
| 85 | F. D. | 80 | 0 | 0 | 0 | |
| 86 | J. F. | 65 | 0 | 0 | 0 | |
| 87 | E. G. | 70 | 0 | 0 | 0 | |
| 88 | I. M. | 70 | 0 | 0 | 0 | |
| 89 | E. K. | 70 | 0 | 0 | 0 | |
| 90 | C. J. | 59 | 0 | 0 | 0 | |
| 91 | R. S. | 78 | 0 | 0 | 0 | |
| 92 | A. K. | 66 | 0 | 0 | 0 | |
| 93 | A. A. | 30 | 0 | 0 | 0 | Chronic glaucoma |
| 94 | C. R. | 51 | 0 | 0 | 0 | |
| 95 | R. W. | 77 | 0 | 0 | 0 | Chronic glaucoma |
| 96 | C. S. | 67 | 0 | 0 | 0 | |
| 97 | W. K. | 79 | 2+ | 0 | 0 | Confused |
| 98 | M. Z. | 71 | 1+ | 0 | 0 | Confused, one eyed |
| 99 | A. M. | 71 | 0 | 0 | 0 | |
| 100 | A. R. | 71 | 0 | 0 | Diabetes | Chronic glaucoma-rubeosis Intraocular hemorrhage |

uncommon. We believe that, since the patient sits up immediately postoperatively and is allowed to turn on the unoperated side, this complication is markedly reduced.

COMMENT

One concludes, by observation, that chlorpromazine exerts a selective inhibitory effect on the functions of the central nervous sys-

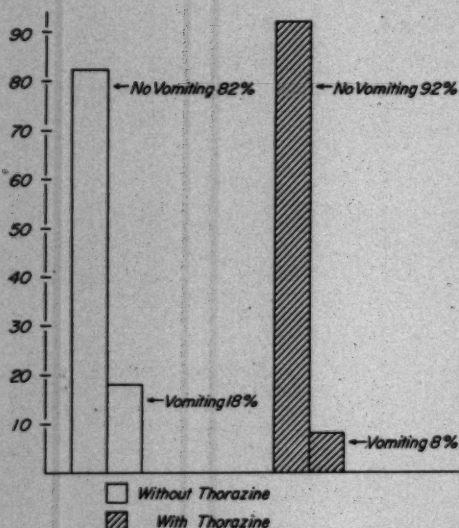


Fig. 3 (Harley and Mishler). Incidence of vomiting with and without Thorazine in 200 consecutive cataract extractions.

tem especially in the field of psychomotor and emotional activity. It may be described as an emotional detachment without clouding of consciousness or disturbance of intelligence. Many of the patients had no recollection of the operation and it was not uncommon for them to ask the surgeon many hours later "When will the operation be performed?" However, in spite of their lethargy and amnesia they usually can be aroused at the time of surgery if it is required. Since chlorpromazine potentiates the premedication it was found that excessive medication preoperatively was possible and could be disadvantageous. During the operation excessive somnolence may be hazardous since frequently the subject is beyond the zone of passive co-operation and may move unexpectedly in his "dream state."

Repeated observation has confirmed the opinion that nausea and vomiting occurring within the first 48 hours is most frequently related to the surgery; whereas, the nausea and vomiting occurring after 48 hours commonly results from medical and, rarely, ocular complications. In view of this observation it appears advisable to continue chlorproma-

zine (25 mg. every six hours) for 48 hours. In this way nausea and vomiting should be still further reduced in incidence. A new series of 100 cataract extractions utilizing this dosage technique is in progress.

REVIEW OF CASES

A review of certain cases illustrates the effectiveness of chlorpromazine:

Case 36. There was nausea and one dose of chlorpromazine immediately relieved it.

Case 44. Vomited on the fifth postoperative day. The patient remained extremely tense and nervous. Chlorpromazine (25 mg.) relieved vomiting and the patient ate within two and one-half hours.

Case 47. Vomited on the third postoperative day. Chlorpromazine (25 mg.) relieved the symptoms. There had been no vomiting prior to the third day. The patient developed severe mental confusion.

Case 58. Developed a severe uveitis the fifth day. The patient was given intravenous typhoid injections and vomited in the absence of chlorpromazine. The drug was eventually given and controlled vomiting.

Case 65. Chlorpromazine (25 mg.) stopped emesis and the patient ate within one-half hour.

Case 77. The patient was nauseated immediately following surgery. Chlorpromazine (25 mg.) relieved nausea.

Case 79. Vomited preoperatively just outside the operating room. Chlorpromazine (25 mg.) intramuscularly stopped emesis and surgery was performed one-half hour later in the absence of further vomiting.

Cases 44, 47, and 58 were not counted

| | Minimal Vomiting | Severe Vomiting | Total |
|----------------------|------------------|-----------------|-------|
| No Thorazine Control | 10 | 8 | 18 |
| Thorazine | 5 | 3 | 8 |

Fig. 4 (Harley and Mishler). Frequency of vomiting in 200 cataract extractions.

in this series since the vomiting occurred prior to the administration of chlorpromazine. However, the drug appeared to be immediately effective when used in these cases.

COMMENT

The chlorpromazine pallor with its resemblance to shock may sometimes give rise to alarm. This appearance generally occurs 30 to 40 minutes after oral medication when the patient becomes calm and relaxed. Ordinarily, the blood pressure drops moderately but the patient remains warm and dry with pink nail beds.¹² If the hypotensive effect should become more severe, elevation of the legs, lowering of the head, and administration of norepinephrine (Levophed) may be necessary. One patient outside of our present series required such treatment.

No case of jaundice occurred on our series. In the estimated seven million patients who have had chlorpromazine in this country the incidence of jaundice irrespective of dosage has been low.¹³ In England and Europe jaundice was noted in three of more than 10,000 patients treated with chlorpromazine (Stewart and Redeker¹⁴). Jaundice appears to be related to duration of treatment since few cases have occurred in less than one week. Chlorpromazine may be contraindicated in patients with known liver disorders.

Agranulocytosis has been reported as a rare complication but nearly all cases have occurred between the fourth and 10th week of treatment.¹⁵

Dermatologic reactions in the form of a mild urticarial eruption have been reported. They are believed to be of allergic origin

and clear promptly upon withdrawal of the drug.¹⁵

SUMMARY

1. An attempt has been made to evaluate the usefulness of chlorpromazine (Thorazine®) in 100 consecutive cataract extractions. The results have been compared with an additional series of 100 consecutive cataract extractions in which chlorpromazine was not used.

2. Chlorpromazine was chosen for evaluation because of its reputed ability to relieve anxiety and reduce the incidence of nausea and vomiting. These two qualities of the drug should be of great benefit in ophthalmic surgery.

3. The tranquilizing effect of chlorpromazine has an impressive therapeutic effect on apprehensive, tense and anxious patients. Improvement with this drug was at least 10 percent more when compared with patient performance under the former premedication.

4. Chlorpromazine successfully reduces severe nausea and severe vomiting during and following cataract surgery. Statistical analysis of these results by the chi-squared technique indicates that the figures are significant.

5. Further investigation may show an improved dosage technique which will further reduce nausea and vomiting. Such a new series is in progress.

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BIOCHEMICAL STUDIES ON CATARACT*

V. BIOCHEMICAL GENESIS OF SENILE CATARACT

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Many authors have reported on the problems of senile cataract. Magnus¹ reported that senile cataract was due to dehydration of the lens fibers. Peters² and Roemer³ described the changes in the components of the aqueous humor due to the degeneration of ciliary epithelium. Kuwahara⁴ reported the accumulation of ammonium bicarbonate in the blood of patients with senile cataract and assumed that the increase in ammonia of the aqueous humor caused cataract.

Burdon-Cooper⁵ observed the decrease in molecular concentration and the decrease in surface tension of aqueous humor of patients suffering from senile cataract. From these observations, he reported the interrelationship between the function of the kidney and genesis of cataract.

Roemer³ assumed that some cytoplasmic toxin which causes the precipitation of lens protein increases in the blood. Friedrich⁶ described the effect of ultraviolet light on the lens protein. Fischer and Triebenstein⁷ found latent tetany in 88.2 percent of cataractous patients and reported that the decrease of calcium in the blood was important in the development of senile cataract. Goldschmidt⁸ described the relationship between the shift of the pH to the acid side and the genesis of cataract.

According to Hektoen and Schulhof,⁹ beta crystallin, one of the soluble lens proteins, is spontaneously precipitable and alpha crystallin prevents this precipitation as a protective colloid. In this case, if alpha crystallin decreases, beta crystallin precipitates immediately and cataract develops. However, Dold, Flossner, and Kutschner¹⁰ denied these observations.

Although many works concerning the genesis of senile cataract have been reported, there is no clear-cut work on the biochemical genesis of senile cataract. During a series of biochemical studies on various experimental cataracts, it was discovered that some quinoid substances, such as beta naphthoquinone in naphthalene cataract,¹¹ benzoquinone-acetic acid in cataract induced by the administration of tyrosine and sodium butyrate,¹² 2-amino-p-quinonimine in dinitrophenol cataract,¹³ and benzoquinone-acetic acid in galactose cataract,¹⁴ act as cataractogenic agents.

Furthermore, it was observed that vitamin-C deficiency and the dysfunction of the liver are closely related to the development of cataract by these quinoid substances. It is well known that ascorbic acid in the aqueous humor and crystalline lens of the patient with senile cataract decreases markedly. Recently, from our results, latent vitamin-C deficiency and disturbance of its oxidoreductive sys-

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TABLE 1
CATARACT PATIENTS WHOSE URINE WAS USED

| Case No. | Sex | Age (yr.) | Cataracta Senilis | | Visual Acuity | | Development of Cataract |
|----------|-----|-----------|-------------------|-----------|---------------|-------------|-------------------------|
| | | | Right | Left | Right | Left | |
| 1 | ♀ | 50 | Incipient | Mature | 0.7 | 0.02 | Before |
| 2 | ♀ | 73 | Mature | Mature | 30 cm./n.d. | 50 cm./n.d. | 3 yr. |
| 3 | ♀ | 81 | Mature | Mature | 20 cm./n.d. | 0.06 | 2 yr. |
| 4 | ♀ | 48 | Mature | Mature | 1 m./m.m. | 50 cm./m.m. | 1 yr. |
| 5 | ♀ | 74 | Mature | Mature | s.l. | s.l. | 3 yr. |
| 6 | ♀ | 50 | Mature | Incipient | 30 cm./m.m. | 0.7 | 10-15 yr. |
| 7 | ♂ | 54 | Mature | Mature | 0.1 | 0.1 | 2-3 yr. |
| | | | | | | | 3 yr. |

tem have been found to exist in the patients with senile cataract.¹⁵

In this paper, an attempt was made to clarify the cataractogenic agent of senile cataract on the basis of these findings and the conclusion was reached that there was an interrelationship between the development of cataract and the abnormal metabolism of tryptophan in the patient with senile cataract.

EXPERIMENTAL STUDIES

1. *Patients with senile cataract.* Seven cases, shown in Table 1, were selected for these experiments. They had no eye symptoms except for cataracts. Wassermann's reaction was negative in all cases. The patients' diet was according to their choice; no drugs were given.

2. *Control cases.* The cases presented in

Table 2-A were all normal and the ages were the same as those of the test group. Visual acuity was 0.9 or more in all cases. The patients shown in Table 2-B all suffered from some ocular disease other than cataract.

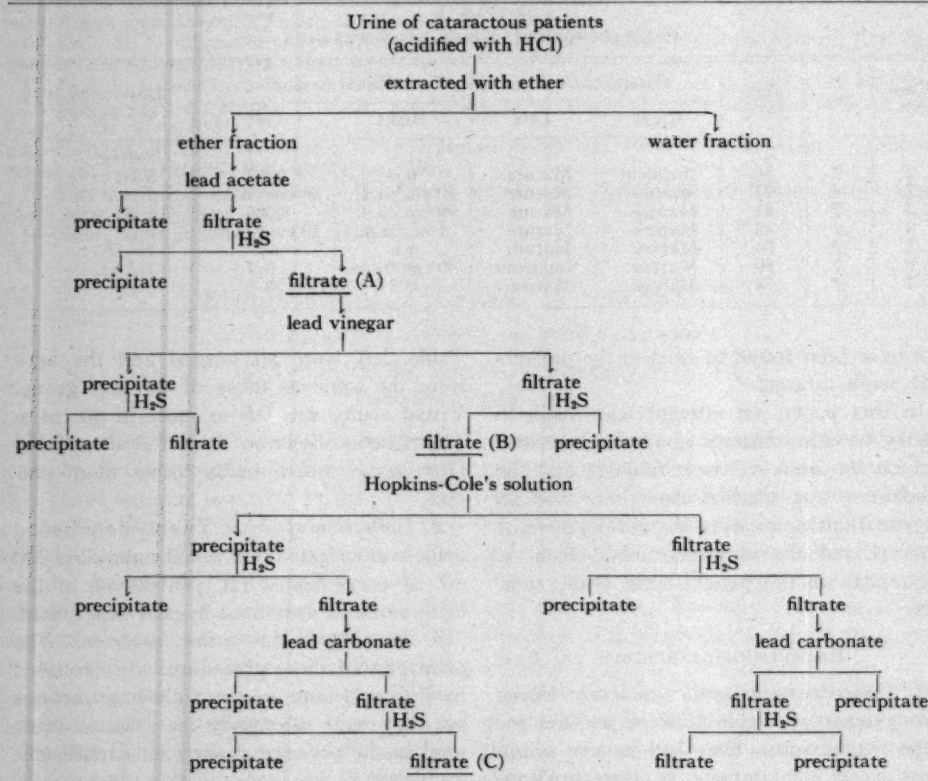
3. *Collection of urine.* Twenty-four hours' urine was collected in a vessel containing 300 ml. of concentrated HCl; 3,000 ml. of the urine samples were used in each experiment.

4. *Procedures for urine treatment.* The principles of these procedures are described in Figure 1 and in the following sections but they were essentially the same as those used in the previous reports on naphthalene cataract.¹¹

5. *Guinea pigs.* Male guinea pigs weighing about 300 gm. were maintained on a basic diet and sufficient vegetables. After feeding for two weeks under these conditions, the

TABLE 2
CONTROL SUBJECTS WHOSE URINE WAS USED

| | Case No. | Sex | Age | Visual Acuity | | Ocular Disease |
|-------------------|----------|-----|-----|---------------|-------------|---------------------------|
| | | | | Right | Left | |
| A. Normal person] | 1 | ♀ | 75 | 1.0 | 1.0 | — |
| | 2 | ♀ | 56 | 1.5 | 1.5 | — |
| | 3 | ♀ | 75 | 1.0 | 1.0 | — |
| | 4 | ♀ | 77 | 1.0 | 1.0 | — |
| | 5 | ♀ | 62 | 0.9 | 1.0 | — |
| | 6 | ♀ | 70 | 1.0 | 1.2 | — |
| B. Patient | 7 | ♀ | 35 | 0.5 (1.0) | 0.5 (1.0) | Strabismus concomit. div. |
| | 8 | ♀ | 60 | 0.7 (1.0) | 0.1 (1.0) | Abscess of orbit |
| | 9 | ♀ | 59 | 0.4 (N.C.) | s.l. (N.C.) | Glaucoma simplex chronic |
| | 10 | ♂ | 59 | 0.1 (N.C.) | 0.5 (N.C.) | Dendritic keratitis |
| | | | | | | |



Underlining denotes the fraction containing the cataractogenic substance.

Fig. 1 (Ogino and Ichihara). Procedures used in this study.

animals which gained in body weight were selected for further experiments on cataract formation.

Vitamin-C deficient diets (well mixed over a water bath) used in these experiments were:

| | |
|----------------------------------|--------------|
| Tofukasu* (autoclaved at 120°C.) | 90.0 percent |
| Casein | 3.0 percent |
| Outer portion of wheat | 5.0 percent |
| Butter | 2.0 percent |
| Water | 100.0 ml. |

6. Injection of treated urine into vitamin-C deficient guinea pigs. The solution at

*Tofu is a Japanese food made of the soluble protein of soya bean. Tofukasu is the insoluble residue.

each stage obtained from various treatments of the urine was adjusted to pH 6.0 to 6.5 and 0.5 to 1.0 ml. of this solution was injected intraperitoneally into scorbutic guinea pigs.

7. *Paper chromatography of the cataractogenic substance.* Identification of the cataractogenic substance excreted in the urine is one of the clues to the genesis of senile cataract.

First, paper chromatography is used to detect the cataractogenic agent. The solvent used in these experiments was n-buthanol containing water and acetic acid (n-buthanol: acetic acid:water 4:1:1). The development time was 15 hours. Identification of the spots

TABLE 3
EXPERIMENTS USING ETHER FRACTION PREPARED FROM CATARACT PATIENTS' URINE

| Case Animal No. | No. 1 | | | | | | No. 2 | | | | | | No. 3 | | | No. 4 | | | No. 5 | | | No. 6 | | | | No. 7 | | |
|-------------------------|-------|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-------|-----|-----|-------|-----|-----|-------|-----|-----|-------|-----|-----|-----|-------|-----|-----|
| | 1 | 2 | 3 | 4 | 5 | 6 | 21 | 22 | 23 | 36 | 37 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 31 | 52 | 53 | 54 | 55 | 56 | 64 | 63 | 86 | 87 |
| 5 | 1.0* | 1.0 | 1.0 | | | | 0.5* | 0.5 | 0.5 | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 0.7 | 0.7 | 1.0 | 1.0 | 1.0 | | | |
| 6 | 1.0 | 1.0 | 1.0 | | | | 0.5 | 0.5 | 0.5 | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 7 | 1.0 | 1.0 | 1.0 | | | | 0.5 | 0.5 | 0.5 | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 8 | 1.0 | (+) | | | | | (+) | (+) | (+) | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 9 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 10 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 11 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 12 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 13 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 14 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 15 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 16 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 17 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 18 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 19 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| 20 | | | | | | | | | | | | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | |
| Vitamin-C Deficient Day | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cataract | (+) | (+) | (-) | (+) | (+) | (+) | (+) | (+) | (-) | (+) | (+) | (+) | (+) | (-) | (+) | (+) | (-) | (-) | (+) | (+) | (-) | (-) | (-) | (-) | (+) | (-) | (+) | (+) |

* Injection doses in ml.
Vitamin-C deficient guinea pigs were injected with ether fraction subcutaneously daily.

TABLE 4
EXPERIMENTS USING ETHER FRACTION PREPARED FROM URINE OF NORMAL PERSONS

| Control Case Animal No. | Cataractous Case | | | | | No. 1 | | | No. 2 | | | Cataractous Case | | No. 3 | | | No. 4 | | | No. 5 | | | No. 6 | | |
|----------------------------|------------------|-----|------|-----|------|-------|-----|-----|-------|-----|------|------------------|-----|-------|-----|------|-------|------|-----|-------|------|-----|-------|--|--|
| | 63 | 64 | 65 | 66 | 67 | 68 | 69 | 70 | 86 | 87 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | | | |
| 8 | 1.0* | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 9 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 10 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 11 | Died | 1.0 | 1.0 | 1.0 | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 12 | | (+) | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | Died | 1.0 | 1.0 | Died | 1.0 | | | |
| 13 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 14 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 15 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 16 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 17 | | | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 18 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 19 | | | 1.0 | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | | | |
| 20 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 21 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 22 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 23 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 24 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 25 | | | | | | | | | | | | | | | | | | | | | | | | | |

* Injection doses in ml.

was carried out by the diazo reaction, ninhydrine reaction, fluorescence, and Rf values on the filter paper.

RESULTS

1. *Extraction with ether.* The problem of initial importance in these experiments is whether or not the cataractogenic substance is excreted in the urine of those patients with senile cataract. First, the ether fraction of the urine was used for this.

Three thousand ml. of urine acidified with concentrated hydrochloric acid was filtered and then extracted with the same amount of ether for 2,000 times or more. The ether was evaporated at low temperature, the residue was dissolved in 50 ml. of water, and the solution obtained was injected into scorbutic guinea pigs.

As can be seen in Table 3, all scorbutic guinea pigs developed cataracts following injection of ether fractions.

2. *Control examination.* After the urine collected from the control subjects had been treated by the same method as in the test experiments, the solution obtained was injected into scorbutic guinea pigs. The development of cataract could not be demonstrated in any of these animals (tables 4 and 5).

From these findings, it can be concluded

that a cataractogenic substance is excreted only in the urine of a patient with senile cataract.

3. *Experiments with lead acetate.* Three thousand ml. of urine were extracted with ether, as already described, and the ether was evaporated. The residue was dissolved in 100 ml. of water, lead acetate was added until no more precipitation occurred, and the mixture was filtered. The precipitate obtained was washed with water repeatedly and dried at room temperature.

Next the pulverized precipitates were suspended in 100 ml. of water and lead was removed with H_2S and the H_2S was expelled by bubbling air. These procedures were carried out two times. The filtrate was treated in the same manner as the precipitate.

Both solutions thus obtained were concentrated to 50 ml. under reduced pressure and were adjusted to pH 6.0 to 6.5. One-half ml. of each solution was injected into guinea pigs from the fifth day of vitamin-C deficient feedings.

The results are presented in Table 6-A. As can be seen from this table, all animals developed cataract following injection of the filtrate but not of the precipitate. In other words, the cataractogenic substance was not precipitable with lead acetate.

4. *Experiments with lead vinegar.* Until

TABLE 5
EXPERIMENTS USING ETHER FRACTION PREPARED FROM URINE OF PATIENTS WITHOUT CATARACT

| Control Case | | Cataractous Case | | No. 7 | | | No. 8 | | | Cataractous Case | | No. 9 | | | No. 10 | | |
|-------------------------|----|------------------|-----|-------|------|------|-------|------|------|------------------|-----|-------|------|------|--------|------|------|
| Animal No. | | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 63 | 64 | 60 | 61 | 62 | 71 | 72 | 73 |
| Vitamin-C Deficient Day | 8 | 0.7* | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 1.0* | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 9 | 0.7 | 0.7 | 0.7 | 0.7 | Died | 0.7 | 0.7 | 0.7 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 10 | 0.7 | 0.7 | 0.7 | 0.7 | | Died | 0.7 | 0.7 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 11 | 0.7 | 0.7 | 0.7 | 0.7 | | | 0.7 | 0.7 | Died | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 12 | 0.7 | 0.7 | 0.7 | 0.7 | | | 0.7 | 0.7 | | (+) | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 13 | (+) | (+) | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 14 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 15 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 16 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 |
| | 17 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | | 1.0 | 1.0 | 1.0 | 1.0 |
| | 18 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | Died | 1.0 | 1.0 | 1.0 | 1.0 |
| | 19 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | 1.0 | | 1.0 | 1.0 | 1.0 | 1.0 |
| | 20 | | | 0.7 | 0.7 | | | 0.7 | 0.7 | | | Died | | 1.0 | 1.0 | 1.0 | 1.0 |
| | 21 | | | 0.7 | Died | | | 0.7 | 0.7 | | | | | 1.0 | 1.0 | 1.0 | 1.0 |
| | 22 | | | Died | | | | 0.7 | 0.7 | | | | | 1.0 | 1.0 | 1.0 | 1.0 |
| | 23 | | | | | | | Died | Died | | | | | Died | 1.0 | 1.0 | 1.0 |
| | 24 | | | | | | | | | | | | | | Died | 1.0 | 1.0 |
| | 25 | | | | | | | | | | | | | | | Died | Died |

* Injection doses in ml.

TABLE 6

EXPERIMENTS USING VARIOUS FRACTIONS PREPARED FROM URINE OF PATIENTS WITH CATARACT

| Procedure | | A: Lead Acetate | | | | | | B: Lead Vinegar | | | | C: Hopkins-Cole's Solution | | | | | |
|-------------------------|----|-----------------|------|------|----------|-----|-----|-----------------|-----|----------|-----|----------------------------|-----|-----|----------|-----|-----|
| Fraction | | Precipitate | | | Filtrate | | | Precipitate | | Filtrate | | Precipitate | | | Filtrate | | |
| Animal No. | | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 24 | 25 | 26 | 27 | 28 | 29 |
| Vitamin-C Deficient Day | 5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | | | | | | |
| | 6 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | | | | | | |
| | 7 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | | | | | | |
| | 8 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 9 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 10 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 11 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 12 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 13 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 14 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 15 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 16 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 17 | 0.5 | Died | Died | | | | 0.5 | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 18 | 0.5 | | | | | | 0.5 | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 19 | 0.5 | | | | | | 0.5 | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 20 | 0.5 | | | | | | Died | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 21 | 0.5 | | | | | | 0.5 | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 22 | 0.5 | | | | | | Died | 0.5 | | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| | 23 | Died | | | | | | | | | | | | | Died | | 1.0 |

Five days after vitamin-C deficient feeding, guinea pigs were injected with various fractions prepared from cataractous patient urine by lead acetate, lead vinegar, and Hopkins-Cole's solution.

no increase in precipitate occurred, lead vinegar was added to the filtrate treated with lead acetate as described, and filtered. The filtrate and precipitate obtained were treated by the same method as in Experiment 3 and were injected into the scorbutic guinea pigs.

As can be seen from Table 6-B, the cataractogenic agent was found in this filtrate.

5. *Experiments with Hopkins-Cole's solution.* To the filtrate obtained in Experiment 4, Hopkins-Cole's solution (10-percent HgSO_4 in five-percent sulfuric acid) was added until there was no more precipitation and then filtered. The filtrate was kept at room temperature for 10 hours and the Hg was removed with H_2S as mercuric sulfide. Then the sulfuric acid was removed by additional lead carbonate and lead was removed with H_2S . After this, the precipitate obtained in Experiment 4 was treated in the same manner as already described.

Both precipitate and filtrate were treated two times as described and 1.5 ml. of each solution was injected into guinea pigs from the fifth day of vitamin-C deficient feeding. The results are presented in Table 6-C.

From these results, it is clear that the cataractogenic substance is precipitated with Hopkins-Cole's solution.

6. Identification of cataractogenic sub-

stance by paper chromatography. The chemical natures of the solutions obtained from Experiment 1 to Experiment 5 are presented in Table 7-A. Next, each urine collected from the six cases of senile cataracts was treated by the methods of Experiment 1 to Experiment 5 and the solutions obtained were analyzed by paper chromatography.

As can be seen in Figure 2, two spots (F_1' , F_2') were detectable on the filter paper by

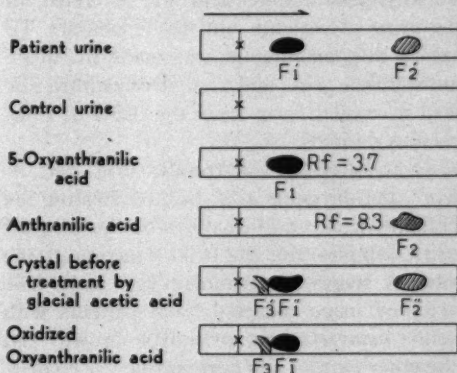


Fig. 2 (Ogino and Ichihara). Paper chromatogram of cataractogenic substance excreted in the urine of cataract patients. (Method of paper-partition chromatography: one dimensional and ascending method; filter paper, Toyo filter paper, No. 52; developer, n-Butanol acetic-acid water (4:1:1); developing time, 12 hours.)

TABLE 7
 CHEMICAL FINDINGS OF ISOLATED CRYSTALS

| Material Reaction | A Fraction Treated with Lead Acetate, Lead Vinegar and Hopkins- Cole's Solution | B Crystals before treatment with Glacial Acetic Acid | C Crystals after treatment with Glacial Acetic Acid | D 5-Hydroxyanthranilic Acid |
|------------------------------|---|--|---|---------------------------------------|
| Melting point | — | — | 230° C | 231° C |
| KJO ₄ | Yellow (ether extractable) | Red-purple (ether not extractable) | Red-purple (ether not extractable) | Red-purple (ether not extractable) |
| Fe ⁺⁺⁺ | Yellow-brown | Yellow-brown | Yellow-brown | Yellow-brown |
| Ammonia | Light brown | Red | Red | Red |
| Ootani-Honda's reagent* | Purple-brown (ether extractable) | Purple-brown (ether extractable) | (—) | (—) |
| Millon's reagent | Red-brown | Pale red | Pale red | Pale red |
| Ammoniacal silver reagent | (+) | (+) | (+) | (+) |
| Ninhydrin | (+) | (—) | (—) | (—) |

* Ootani-Honda's reagent: Paradimethylaminobenzaldehyde and hydrogen peroxide (Osaka M. Ass., 37: 1-10, 1938).

the fluorescence and diazo reactions. Of these spots, F_2' was found in two cases (4, 7) and was not clear in the other four cases (1, 2, 3, and 5). From the chemical natures and the R_f values of these spots, it may be concluded that these two spots (F_1' , F_2') are compatible with 5-hydroxyanthranilic acid (R_f : 3.7 to 5.5) and anthranilic acid (R_f : 8.3 to 9.5). On the other hand, the control urine treated as described, did not give these spots.

These data suggest that anthranilic and 5-hydroxyanthranilic acid are excreted in the urine of patients with senile cataract. To verify this, an attempt was made to isolate anthranilic acid and 5-hydroxyanthranilic acid in crystal form from the urine of cataractous patients.

7. Isolation of anthranilic acid and 5-hydroxyanthranilic acid. Before isolating the crystals, a chemical analysis of the original urine samples and the urine fraction at the various stages of treatment was done. The acidified urine collected from patients with senile cataracts was red-purple-brown, and the ether extract was deep purple. In Experiment 3, Experiment 4, and Experiment 5, the pale-yellow solution obtained after the removal of Pb with H_2S became orange-yellow after bubbling air through it for a long time. The original color was never regained by reduction with H_2S .

The isolation of 5-hydroxyanthranilic acid and anthranilic acid from the urine of patients with senile cataracts was carried out by Kotake and Shirai's method.¹⁶

Twelve liters of urine were collected in a vessel containing 100 ml. of 30-percent acetic acid per 100 ml. of urine. This was filtered repeatedly and then concentrated to 750 ml. under reduced pressure at 45°C. Lead acetate was added to this concentrated urine until no more precipitate occurred and then was filtered. The filtrate was bubbled with H_2S to remove Pb and filtered. The filtrate was concentrated to 15 ml. under reduced pressure and was extracted with the same amount of ether for 10 hours. After the ether was evaporated, 100 ml. of alcohol were added to the residue and evaporated in vacuum. These procedures were carried out two times, then water was added to the residue and dried in vacuum. The residue was extracted with warm ether and ether was evaporated.

Orange-brown crystals were obtained after evaporation of the ether. The crystals recrystallized with water, were pale purple-white and amorphous (fig. 3). The various color reactions of these crystals are presented in Table 7-B.

These crystals were separated into two spots (F_1'' , F_2'') on the filter paper, agreeing with those of anthranilic acid and 5-hydroxy-

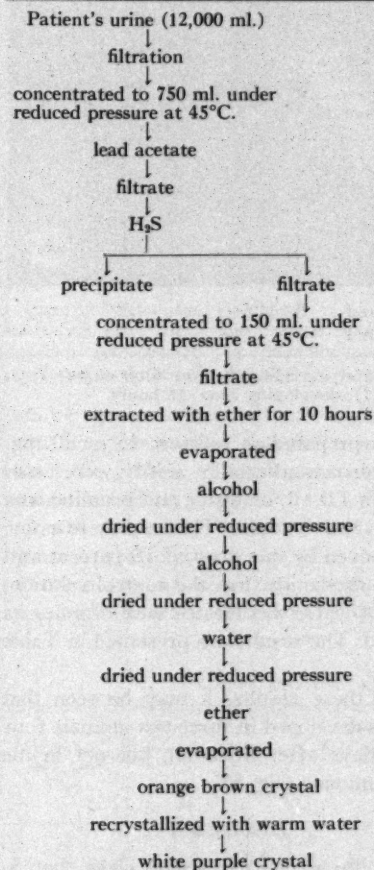


Fig. 3 (Ogino and Ichihara). Isolation of cataractogenic substance.

anthranilic acid (F_1 , F_2 , fig. 2, table 8). In this case, one more spot (F_3') was detectable on the filter paper, but it could not be determined exactly. However, this spot (F_3') agreed with that (F_3) of 5-hydroxyanthranilic acid oxidized with bromine (table 8).

Following this, the crystals obtained were dissolved in glacial acetic acid and filtered. The insoluble crystals were repeatedly washed with ether and dried in vacuum. About 10 mg. of white-yellow crystals were obtained. These crystals were shaped like little cones or were amorphous.

As can be seen in Table 7-C, the color reactions of these crystals agreed completely with those of 5-hydroxyanthranilic acid.

The melting point of these crystals was 230°C . (capillary method) and this melting point did not drop by mixing with pure 5-hydroxyanthranilic acid. The values of the N analyses of these crystals were as follows:

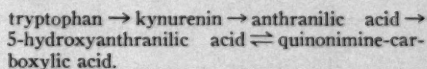
Materials = 3.817 mg.
 $N = 0.292$ cc. (18.5°C ., 764.3 mm.Hg)
 Experimental value: $N = 8.82$ percent
 Theoretic value: $N = 9.15$ percent

From these results, it can be concluded that these crystals are 5-hydroxyanthranilic acid.

Furthermore, about 25 mg. of anthranilic acid were obtained from the soluble fraction in glacial acetic acid. Anthranilic acid was identified with Nishikawa's test¹⁷ and by its melting point (142°C .) (standard melting point is 145°C).

These results seem to show that both anthranilic acid and 5-hydroxyanthranilic acid are excreted in the urine of patients with senile cataract.

8. *Cataractogenic activity of quinonimine-carboxylic acid.* The following system for the metabolism of tryptophan has already been established by Kotake¹⁸:



The latter two substances are interchangeable by adding or removing two hydrogen atoms respectively and form a redox system (fig. 4). Moreover, there is no evidence of the excretion of 5-hydroxyanthranilic acid in human urine without additional tryptophan or anthranilic acid.

In our results, also, 5-hydroxyanthranilic acid was not detectable in the urine of normal persons but this acid could be obtained from the urine of patients with senile cataracts. Furthermore, it was shown that scorbutic guinea pigs developed cataracts following injection of the fraction obtained from urine containing 5-hydroxyanthranilic acid. In addition, it has previously been reported that



Fig. 5 (Ogino and Ichihara). (A) Cataract in guinea pig following injection of quinonimine-carboxylic acid, one of the intermediates of tryptophan. Test animal No. 35, eight days after vitamin-C deficient feeding; 15 mg. quinonimine-carboxylic acid were injected subcutaneously daily. Cataract developed on the seventh day of the experiment. (B) Control animal No. 92.

cataractogenic activity. Therefore, these results suggest a close interrelationship between the genesis of senile cataract and the metabolism of tryptophan.

On the other hand, as previously reported by us, scorbutic guinea pigs develop cataract as the result of abnormal metabolism of tyrosine.¹² However, the relationship between

the abnormal metabolism of tyrosine and the genesis of senile cataract must be left for future studies.

SUMMARY

1. Although a cataractogenic substance is excreted in the urine of patients with senile cataract, it is not in that of normal persons.

TABLE 9
CATARACTOGENIC ACTIVITY OF QUINONIMINE-CARBOXYLIC ACID

| Vitamin-C Deficient Day | Test | | | | Control | | |
|-------------------------------|--------------------------|------|------|------|---------|------|------|
| | Experiment Animal Number | | | | | | |
| | 34 | 35 | 88 | 89 | 90 | 91 | 92 |
| 8 | 1.0 | 1.0 | | | | | |
| 9 | 1.0 | 1.0 | | | | | |
| 10 | 1.0 | 1.0 | 1.0* | 1.0* | 1.0 | 1.0 | 1.0 |
| 11 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| 12 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| 13 | Cat. | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| 14 | | Cat. | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| 15 | | | Died | Cat. | 1.0 | 1.0 | 1.0 |
| 16 | | | | | 1.0 | 1.0 | 1.0 |
| . | | | | | . | . | . |
| . | | | | | . | . | . |
| 19 | | | | | Died | 1.0 | 1.0 |
| . | | | | | | . | Died |
| . | | | | | | . | |
| . | | | | | | . | |
| . | | | | | | . | |
| 24 | | | | | | Died | |

* Test group. The test group was injected with 15 or 20 mg. of quinonimine-carboxylic acid subcutaneously and the control group was injected with the same amount of water treated with the same method as in the preparation of quinonimine carboxylic acid. Quinonimine carboxylic acid was prepared as follows; 15 to 20 mg. of 5-hydroxyanthranilic acid was suspended in 1.0 ml. of water and bromine was added as an oxidant. Excess bromine was expelled by bubbling with air for 15 minutes.

2. This cataractogenic substance is extractable with ether under acidified conditions and can be precipitated with Hopkins-Cole's solution as mercuric compounds but it is not precipitable with lead acetate and lead vinegar.

3. Anthranilic acid and 5-hydroxyanthranilic acid are detectable by paper chromatography from the fraction precipitated with Hopkins-Cole's solution.

4. 5-hydroxyanthranilic acid and anthranilic acid can be isolated from the urine of

cataractous patients in crystalline form. For the identification of these substances, the melting point, N analyses, its R_f value, and various color reactions were examined.

5. Scorbutic guinea pigs develop cataracts following injection of quinonimine-carboxylic acid prepared from 5-hydroxyanthranilic acid by bromine.

6. The relationship between the development of senile cataract and the metabolism of tryptophan is discussed.

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NOTES, CASES, INSTRUMENTS

A DEVICE FOR THE DEMONSTRATION AND ANALYSIS OF OCULAR ROTATIONS*

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A number of articles have appeared within the past decade on the interrelationships between the various ocular rotations. To what degree torsion about the anterior-posterior axis takes place when an eye assumes an oblique direction of gaze has received considerable attention. Some authors have insisted that all the torsion is only apparent, while others are equally convinced that true torsion does take place.

In an effort to analyze this problem mathematically, it was decided to construct a simple model which would permit continuous rotations in all planes, with scales to indicate all of the pertinent angles quantitatively. The expense of having the parts made to order seemed rather prohibitive. However, a government surplus navigating compass¹ was adapted to serve as a convenient substitute. Two of these instruments were stripped of the unnecessary attachments and mounted together. A painted wooden hemisphere was

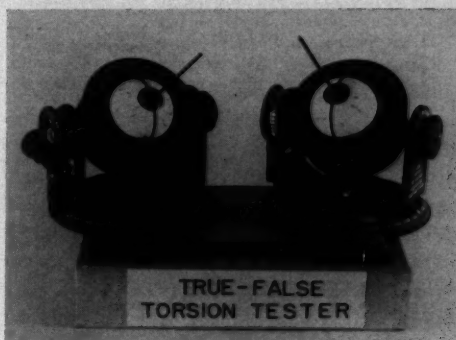


Fig. 1 (Askovitz). A quantitative ophthalmotrope, fastened to each compass assembly, as shown (fig. 1).

It is possible to rotate either "eye" independently, about a horizontal, vertical, or sagittal axis. Each rotation can be read to the nearest degree of arc on the corresponding scale of the instrument.

In addition to its use in investigating true and false torsion, the apparatus shown has also provided a simple means for demonstrating to students of ophthalmology combinations of ocular rotations. Versions, vergences, and torsions are readily clarified by setting the two "eyes" accordingly.

Various other ophthalmotropes have been reported in the literature.²⁻¹³ The most recent of these was shown at Dr. Pascal's exhibit on torsion.¹³

York and Tabor Roads (41).

* From the Ophthalmology Research Laboratory (Dr. I. H. Leopold, Director), Albert Einstein Medical Center, Northern Division. This work was supported by a grant from the Weinstock Fund.

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ATOPIC KERATOCONJUNCTIVITIS*

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Atopic keratoconjunctivitis was first described as a clinical entity by Hogan† who published five case reports in 1952. Following is the report of a similar case in which the diagnosis was clear-cut and in which a successful corneal transplant was obtained.

CASE REPORT

The patient was a 31-year-old white man who complained of chronic swelling and inflammation of both eyes with severe loss of vision of 10 years' duration. He had eczema in childhood but otherwise had not been bothered with skin difficulty until 1943. At this time he developed severe atopic dermatitis manifested by redness, scaling, weeping, and lichenification of the skin of the face, neck, upper trunk, and antecubital and popliteal spaces. Following the initial attack there were remissions but never complete absence of this disorder.

The ocular disturbance of corneal ulceration and scarring and conjunctivitis with thick mucous discharge began in 1946, followed by exacerbations in 1949, 1951, and 1952, each time associated with a flare-up of the dermatitis.

Ocular examination in 1952 revealed mod-

erate conjunctival injection with a thick mucoid discharge. There was an old healed scar involving the central corneal stroma of the right eye reducing vision to 20/100. Approximately two thirds of the corneal epithelium of the left eye stained with fluorescein. Deep infiltrations limited vision to counting fingers.

Treatment consisted of cortisone and atropine eyedrops and systemic cortisone. By the time the patient was discharged one month later his vision had improved to 20/300 in the left eye. Following this severe episode the eye condition was relatively quiescent except for occasional burning, itching, and discharge, particularly when the dermatitis became aggravated. These minor flare-ups were controlled by local cortisone drops.

The patient was referred for corneal transplant in January, 1956. Physical examination revealed an alert, well-developed, and well-nourished 31-year-old white man. The nasal mucous membrane was pale and boggy with a few small polyps present. There was lichenified and excoriating skin of the trunk, upper extremities, and areas behind the ears which was attributed to atopic dermatitis in a quiescent state. The Dermatology Department agreed with this diagnosis and a skin biopsy was compatible with it.

The eye examination showed the lids and conjunctiva to be normal. There was a central haziness of the interstitial layers of the right cornea with a fairly clear periphery. Both superficial and deep blood vessels and ghost vessels extended into the center of the

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cornea. In the left cornea there was a dense scar involving the pupillary area, which extended through the entire thickness of the stroma. The periphery of the cornea was clear except for a few small superficial blood vessels extending one to two mm. toward the center. Visual acuity of the right eye was 20/70, improved with a pinhole to 20/40. Visual acuity of the left eye was 3/200, improved with a pinhole to 20/50-2. The remainder of the ocular examination was not remarkable. The remainder of the general physical examination was within normal limits. Routine laboratory tests and chest X-ray studies were normal except for a 12-percent blood eosinophilia.

On January 13, 1956, the patient was taken to surgery where a corneal transplant was performed on the left eye. A seven-mm. penetrating graft was transplanted using direct sutures. The operation and early postoperative course were uncomplicated. During the immediate postoperative period the patient was kept on oral prednisone up to 40 mg. daily, plus hydrocortisone eye drops. On February 9, 1956, one month after surgery, the vision could be corrected to 20/30, and subsequently to 20/20. Steroid therapy was slowly withdrawn.

During the third postoperative month the operated eye became irritable, there was a mucoid discharge, and the vision was reduced to 20/70. The conjunctiva was slightly edematous and injected. There was fine, superficial, punctate staining of the entire corneal epithelium of the left eye. Conjunctival scrapings showed eosinophilic and polymorphonuclear leukocytes. The patient was started on 20 mg. of prednisone orally per day and neomycin-hydrocortisone ointment locally every two hours. The corneal staining did not disappear, however, until the treatment was changed to 2.5-percent hydrocortisone with one-percent methylcellulose drops and prednisone was increased to 30 mg. daily. Steroid therapy was again withdrawn without recurrence of corneal staining. Improvement to 20/20 vision was sustained.

This patient's case is similar to those reported by Dr. Hogan. In his series there was bilateral keratoconjunctivitis which often had exacerbations concomitant with relapse of the skin disorder. The conjunctiva was thickened and injected while scrapings usually demonstrated eosinophils. There was a mucous discharge and at times an associated staphylococcal infection. Eventually there was corneal involvement, the superficial peripheral portions becoming cloudy first. The epithelium overlying affected areas became edematous with a tendency toward vascularization. Generalized corneal clouding occurred if the condition became severe. The keratoconjunctivitis was usually fairly well controlled by topical and systemic steroid therapy. Severe corneal scarring in two cases necessitated corneal transplantation resulting in improved vision. Dr. Hogan stated that as far as could be determined, no previous cases of keratoconjunctivitis associated with atopic dermatitis were reported in the literature.

COMMENT

This is the sixth case of keratoconjunctivitis associated with atopic dermatitis to be reported. This case parallels the five reported by Dr. Hogan and should further confirm the existence of such an entity. It is noteworthy that good results can be expected from corneal transplant operations. It is also interesting to observe that the grafted cornea apparently reacts in the same manner as the cornea of the host to atopic keratoconjunctivitis. Acute episodes of the disease may be controlled by combined local and systemic steroid therapy.

1033 Gayley Avenue (24).

NAFFZIGER'S ORBITAL DECOMPRESSION*

ITS APPLICATION IN TREATING A CASE OF
OSTEOMYELITIS OF THE ROOF OF THE ORBIT

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The following case is reported to record the success of Naffziger's orbital decompression in treating an intractable osteomyelitis of the roof of the orbit which caused progressive proptosis. As far as can be ascertained, this disease as an indication for this operation has not been reported previously.

REPORT OF CASE

C. B., a boy, aged six years, was admitted to Irwin Hospital on April 1, 1955, with the history of a rapidly increasing proptosis of the right eye for the last six weeks following an attack of fever lasting three days.

Examination showed thickening of the outer half of the right supraorbital margin. There was proptosis of the right eye which was painless and irreducible, causing a forward and downward displacement of the

* From the Irwin Hospital.



Fig. 1 (Jain, Sethi, and Mahajan). Appearance of patient before operation.



Fig. 2 (Jain, Sethi, and Mahajan). Appearance of patient after operation.

globe. Ocular movements and fundi were normal. There was circumcorneal injection and the vision in this eye was slightly impaired, due to a faint superficial corneal opacity. On April 4, 1955, the total WBC count was 16,200, with polymorphs 76 percent, lymphocytes 22 percent, and eosinophils two percent. Erythrocyte sedimentation rate was 32 mm. the first hour (Westergren). Ear, nose, and throat examination revealed no abnormality. Skiagrams were done on April 7, 1955, and showed "hyperostosis of the lesser wing of the sphenoid on the right side."

The patient was put on streptomycin injections (0.25 gm.) and isonicotinic hydrazide (50 mg. twice a day). The eye was kept bandaged. On May 8, 1955, the proptosis had decreased and the patient was discharged relieved.

He was brought back on June 22, 1955, with an increased proptosis and a discharging sinus in the upper-outer angle of the orbit. The probe went almost two inches deep

along the ventral surface of the orbital roof and showed no connection with the lacrimal gland or the frontal sinus. The skin was tender and adherent to the underlying bone with granulation tissue around the opening of the sinus. The conjunctiva was congested and the cornea showed an exposure keratitis with a central corneal ulcer. The erythrocyte sedimentation rate was 85 mm. the first hour (Westergren) and the total WBC count 16,800, with polymorphs 76 percent, lymphocytes 23 percent, and eosinophils one percent.

A median tarsorrhaphy was performed and the patient put on procaine penicillin (400,000 units) with 0.5 gm. streptomycin daily. He improved a little and the corneal ulcer healed quickly.

On July 14, 1955, it was decided to scrape the granulations along the ventral surface of the roof of the orbit. An incision was made concentric with the outer half of the supraorbital margin passing through the sinus and the soft structures were retracted downward, away from the orbital roof. Palpation revealed an eroded and irregular but



Fig. 3 (Jain, Sethi, and Mahajan). Skiagram, showing the four burr holes.



Fig. 4 (Jain, Sethi, and Mahajan). Lateral view of the orbit, showing thickened roof before the operation.

markedly thickened roof, almost up to the apex. With a rougine this was scraped off as much as possible and, with a hammer and gouge, bony pieces, about a quarter inch thick, were removed from the more thickened areas. Granulations along the sinus track were excised, a drainage tube was left in, and the wound was sutured. Pressure dressings and postoperative antibiotics were given.

On July 25, 1955, the sinus and the wound had healed completely, though there was no appreciable decrease in the proptosis. Investigations done now showed erythrocyte sedimentation rate to be 60 mm. the first hour (Westergren), total WBC count 16,500, with polymorphs 59 percent, lymphocytes 40 percent and eosinophils one percent. Antibiotics were continued but on September 6, 1955, a sinus reappeared at its original site. With continued antibiotics, the erythrocyte sedimentation rate came down to 10 mm. the first hour (Westergren) and the total WBC count was 6,000, with polymorphs 59 percent, lymphocytes 38 percent, large mononuclears two percent and eosinophils one percent.

Proptosis with its threatened corneal ulceration and the sinus were now the chief cause of anxiety, and we decided on an orbital



Fig. 5 (Jain, Sethi, and Mahajan). Lateral view of the orbit after operation.

decompression (a) to save the eyeball, the motility, the fundus, and the vision which were satisfactory throughout his illness and (b) to remove the necrosed bone in the roof, since removal of a sequestrum is a sound surgical procedure without which the sinus could not be expected to heal.

Naffziger's orbital decompression and a temporary tarsorrhaphy were performed on September 16, 1955, under general anesthesia. A pressure dressing was applied and a blood transfusion given. The patient became fully conscious in 60 hours and completely afebrile in five days under continued antibiotic therapy. The only significant point during the removal of the orbital roof was the piecemeal removal of necrosed bone.

Recovery was complete and totally uneventful and on September 27, 1955, the total WBC count was 8,500, with polymorphs 69 percent, lymphocytes 28 percent, large mononuclears two percent, and eosinophils one percent. The erythrocyte sedimentation rate was 23 mm. the first hour (Westergren).

There was a slight cicatricial ectropion of the upper eyelid for which a sliding skin graft was applied. The patient was discharged on November 21, 1955, completely cured of the sinus, with proptosis reduced by five mm. His condition has remained satisfactory to date.

DISCUSSION

Extreme proptosis, from causes other than endocrine disorders, which has been treated by Naffziger's orbital decompression does not appear to have been reported in the literature.

Analyzing 78 cases, Guyton has given the following indications for this operation: (a) imminent visual loss in 59 cases due to corneal ulceration, field contraction, and papilledema; (b) diplopia due to impaired ocular mobility in 18 cases; and (c) cosmetic reason in one case.

In our case there were three indications for undertaking this operation particularly when the conservative measures and scraping had failed: (a) Preservation of vision against loss threatened by corneal ulceration due to progressive proptosis; (b) eradication of the disease; and (c) cosmetic value.

Although Guyton favors the operation for cosmetic reasons, Poppen and Naffziger condemn it because of the risks involved. The value of Naffziger's decompression has so far been recognized as purely palliative, since it has been recommended by Naffziger himself and others for treating malignant exophthalmos only. Our case is the one example of the definite therapeutic value of this operation, even if the cosmetic indication is disregarded.

The complications likely to occur in such a drastic operation can be manifold, even resulting in death. In Poppen's 28 cases signs of frontal lobe trauma were seen in three, the longest state of coma lasting for four weeks in one case. The patient under discussion was comatose for 60 hours only. Pulsations of the frontal lobe on the eyeball, reported by Naffziger himself, were not present in this case. Although in operating upon an obviously infected field, there were considerable chances of postoperative meningitis and orbital infection, fortunately none occurred in our case. The only complications met with were irregular pyrexia lasting for five days and a postoperative traumatic re-

action causing temporary increase in proptosis.

SUMMARY

A case of osteomyelitis of the roof of the orbit is presented to record what may be the first nonendocrine indication for Naffziger's orbital decompression.

21 *Faiz Bazar* (7).

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DUOCHROME TELEVISION EYE EXERCISER*

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An entertaining and agreeable method of performing an otherwise monotonous type of eye exercise, for the purpose of attaining useful binocular vision, is overcome to a large degree by the use of the Duochrome Television Eye Exerciser.[†]

The Duochrome Television Eye Exerciser is a red and green plastic cover which is hung in front of the television screen and used with red and green exclusion spectacles, and prism bars (fig. 1).

The red and green strips which are of the same color intensity as those employed in the Three Character Test,¹ used for studying binocular vision, are mounted on a sheet of thin transparent plastic for strength and to facilitate handling. A circular opening 10 cm. in diameter, eccentrically placed, extends equally into the red and



Fig. 1 (Berens, Brackett, and Taylor). Patient enjoying favorite TV program while performing diverging and converging exercises, using the plastic red and green Duochrome Cover with aperture, red-green spectacles, and vertical and horizontal prism bars.

green sections. A rubber suction cup is attached to each corner of the cover to secure it firmly to the television screen.

The red and green duochrome cover with the aperture is placed in front of the television screen, and the red-green spectacles, which exclude the other color for each eye, are worn by the patient. The only part of the screen which can be seen with each eye simultaneously is the central aperture. If two round apertures are seen, a horizontal prism bar² is used, and if hyperphoria exists, a vertical prism bar³ is also used, until the circles are superimposed. When fusion is stable, converging, diverging, and supra-verging exercises may be carried out as prescribed. The prism rack or racks are manipulated gradually to increase the prism strength before the eyes until fusion is broken and doubling of the circle occurs.

In cases of suppression or amblyopia, the Duochrome Television Cover should be attached to the television screen so that the red portion covers the upper half of the screen. The reversible red and green spectacles are worn with the red lens before the suppressing or amblyopic eye.

The advantage of this method of exercise is that fusion exercises may be carried out while the patient is being agreeably enter-

* Aided by a grant from The Ophthalmological Foundation, Inc., and the Department of Research of the New York Association for the Blind and the New York University Post-Graduate School of Medicine, Department of Ophthalmology.

† Made by R. O. Gulden, Philadelphia 20, Pennsylvania, in sizes to fit any TV screen.

tained. Children and even some adults enjoy this form of exercise which before had been considered a monotonous task. Although other observers viewing the screen without colored glasses may find some degree of in-

terference in the picture's reception, nevertheless, the program also may be enjoyed by persons who are not exercising.

708 Park Avenue (21).

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TETANUS INFECTION OF CORNEA*

ITS TREATMENT WITH ACHROMYCIN

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Tetanus infection of the eyeball or eyelid after penetrating lesions has been reported frequently. Corneal tetanus, however, has been reported rather rarely. Dellaporta¹ reported one case after perforating corneal injury and Addario² two cases, one of which resulted in the death of the patient by tetanic paralysis. Quentin³ observed an apparently unique instance in which tetanus occurred following a foreign-body injury that affected only the cornea. The following interesting case showed good results with achromycin and tetanus antitoxin treatment.

CASE REPORT

History. On February 14th, a boy, aged four years, fell from a bicycle and hit his right eye. He was treated by a local doctor and a piece of stone was picked out from the conjunctival sac. However, marked swelling of the lids and conjunctiva with much sticky discharge appeared after a few days. The lid could not be opened. The swelling extended to the right cheek and there was slight fever. The patient appeared at our

clinic on February 20th, six days after the injury.

Eye examination. There were marked swelling and edema of the right lids. The lids could not be opened because of the intensive swelling and pain. The conjunctiva showed an extensive chemosis and hyperemia and covered the cornea. The globe was pushed forward by orbital inflammation.

The upper lateral quadrant of the cornea was opaque and edematous. Only the limbal edge of the corneal lesion stained with fluorescein. The other parts were remarkably elevated but epithelial defects could not be demonstrated by fluorescein. Movements of the eye were completely disturbed.

The very shallow chamber meant a leakage of aqueous humor from the ulcerated cornea. The iris, which was attached to the posterior surface of the cornea, could not be seen clearly because of corneal infiltration. Neither macroscopic penetration of the cornea nor hypopyon could be found (fig. 1).

General anesthesia was given for localization of a foreign body in the deeper portion of conjunctival sac and orbit. A piece of wood, 15 by 10 by 8 mm. with peaked edge, was picked up from the deeper portion of the temporal conjunctival sac. Perforation of the conjunctiva into the orbit was demonstrated at this area. Further X-ray examination for foreign bodies was negative.

Bacteriologic examination. Conjunctival secretion and a piece of necrotized cornea were cultivated on plate and slant blood-agar,

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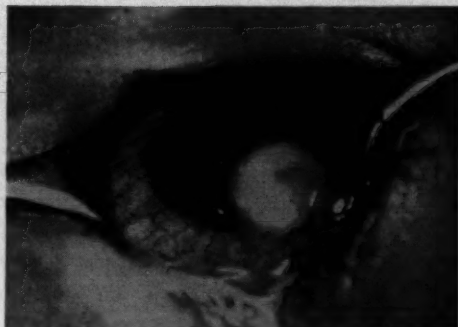


Fig. 1 (Tsutsui). Characteristic appearance of corneal tetanus.

thioglycolate infusion and its agar slant. The blood-agar plate showed no growth but the blood-agar slant showed a little growth in the deep layer of the media, showing a gas bubble in the bottom of the tube. Thioglycolate agar slant showed a typical anaerobic growth and gas formation in its deeper layer. Thioglycolate infusion also showed a typical anaerobic growth in the bottom layer.

Microscopic examination demonstrated *Tetanus* bacilli, showing the typical morphology of gram-negative rods with round and terminal spores. To make a choice of antibiotics, sensitivity of this bacteria was determined. Stab culture was made on thioglycolate agar and, keeping a routine ophthalmic concentration, several drops of each antibiotic solution were instilled on the surface and stabbed again. Gas formation was checked after 24-hour incubation. This strain was sensitive to achromycin, aureomycin, penicillin, and terramycin. Streptomycin, chloramphenicol, and erythromycin could not inhibit its growth.

Treatment and clinical course. The patient entered the hospital and topical instillation of achromycin suspension with compound F was started on the first day. On the second day, bacterial culture showed *Tetanus* bacilli.

Corneal necrosis progressed and a part of the ulcerated portion showed a descemetocoele. Removal of the necrotized layer and thermocoagulation were attempted in order to prevent further anaerobic growth of the *Tetanus*

bacilli. The characteristic picture of this corneal lesion was necrosis of the deep corneal stroma covered with edematous but not necrotized cornea. At operation these layers were completely removed.

For prevention of generalized symptoms, antitoxin was injected from the second day to the fourth day. To inhibit the growth of *Tetanus* bacilli in the deep portion of the orbit and surrounding tissue, oral administration of achromycin (250 mg. daily) was continued for two weeks, as well as topical instillation of atropine and achromycin.

After operation, there was no more extension of corneal infiltration or necrosis but the shallow chamber and deep ulceration of the operated area lasted for two weeks. Regeneration of the ulcerated area occurred in the third week and epithelization was completed in the fourth week. Corneal edema and infiltration around the ulcerated area cleared but a dense adherent leukoma was seen after the inflammation had completely disappeared. The patient was carefully watched for generalized tetanus symptoms which never appeared. On the third day, smear cultures from the surface of the corneal ulcer showed no more growth of *Tetanus* bacilli.

SUMMARY AND COMMENT

This is a relatively favorable case of corneal tetanus, retaining only an adherent leukoma. I noticed a peculiar corneal lesion which I had never seen in other diseases. Widely undermined edges, small epithelial defects, and elevated edematous stroma are characteristic in the early stages of corneal tetanus.

Since the corneal stroma perform anaerobic metabolism, the growth of *Tetanus* bacilli in this layer and rapid extension of the lesion may be expected. Removal of the upper layer of the affected area and exposure to the air are necessary, as are antibiotic treatment and antitoxin injections.

Topical and systemic administration of achromycin was effective in inhibiting further growth of *Tetanus* bacilli and were able

to clear the organisms from the corneal lesion in three days. The minimum concentration of achromycin needed to inhibit the growth of *Tetanus bacilli* was 0.1 per cc. Some other antibiotics, such as aureomycin, penicillin, and terramycin, showed antibiotic action to this organism but some others, such as streptomycin, chloramphenicol, and erythromycin, were not effective.

In this case, unfortunately, as the patient appeared at our clinic six days after he was hurt, antibiotic treatment was started a little late. The corneal lesion was moderately ex-

tended but adequate use of achromycin and tetanus antitoxin followed the prompt bacteriologic diagnosis and sensitivity tests and completely prevented the further extension of corneal ulcer or generalized tetanus symptoms, which sometimes bring death.

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ACKNOWLEDGMENT

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ANKYLOBLEPHARON FILIFORME ADNATUM

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Hasner¹ (1881) was the first to describe a case of ankyloblepharon filiforme adnatum. De Haas² described a similar case in 1896, in which a number of bands of tissue attached to the intermarginal space united the lids. He designated it as *membrana palpebralis perseverans*. Since then 13 such cases have been reported, the last being in 1955 by Lasky.³

CASE REPORT

A 10-day-old Hindu girl was admitted to the Gandhi Memorial and Associated Hospital on September 21, 1954, for inability to open her eyes properly. She was of average weight and full-term normal delivery. Her older sister had had similar trouble, cured by an operation. No other member of the family, either on the maternal or paternal side, is reported to have had such a lesion.

General examination showed her heart to be normal. Except for the harelip and cleft palate, there were no other congenital abnormalities.

Eye examination. The eyebrows were normal. Lids were normal in size and development. The lid margins were connected with a fine elasticlike band, brownish in color, extending from in front of the gray line to the gray line below. Lashes were normal in number, direction, and size. The lid margins could be forcibly separated and, when stretched, brownish, shiny bands could be seen.

In the right eye they were in the region of the junctions of the middle with the lateral and medial thirds; while in the left eye, they extended irregularly over the whole lid margins. In both eyes the canthi were free from these bands.

These bands, when cut with a knife, bled slightly. The bleeding stopped by itself. There was rapid shrinkage of the cut ends of the bands and, within a short period, there was complete disappearance of the vestigial tissue. The rest of the eyes and their adnexa were normally developed. The patient was discharged as cured on September 25, 1954.

Ankyloblepharon filiforme adnatum is characterized by localized, narrow, bandlike union between the two lids, which reduces the palpebral fissure by interfering with the

movements of the lids. It differs from other types of congenital ankyloblepharon by having fine bands of extensible tissue instead of the direct adhesion of the lid margins by the continuation of the skin or by development of connective tissue and vascular structures between the lid margins. Thus, the lid margins could be separated by forcibly stretching the bands, sometimes even to double their normal length. Separation of the lid will depend on the number, location, and extensibility of these bands and the force used to separate them.

The bands may be single or multiple. They may occur in one or both eyes, and may or may not be symmetrical. They may be seen on the lateral, middle, or, very rarely, on the nasal side but never at the canthi. They are fairly elastic and have skin on the outer surface and conjunctiva on the inner surface. The length of these bands varies from one to 10 mm. and the width from 0.3 to 0.5 mm. They are attached to the lid margins between the cilia and orifices of the tarsal glands.

Microscopic examination according to Duke-Elder⁴ shows central vascular connective-tissue strands surrounded by pavement epithelium. Connective tissue is highly cellular and embryonic in nature but Cordero⁵ found muscle fibers and numerous subepithelial glands.

Sectioning of the bands causes bleeding which may be brisk but limited. There is a rapid shrinkage of the cut parts of the bands, with rapid and complete disappearance of all vestiges of excess tissue. Most of these bands are situated in the lateral half, only a few are on the nasal side. Bunzel⁶ and Webster⁷ reported cases having bilateral occurrence of a single band.

There is no definite relationship to prematurity. Only Wintersteiner's⁸ case out of the 14 reported cases was in a premature infant (seven months). Very occasionally the condition appears to be hereditary. There is no sex-linked characteristic. Unlike ankyloblepharon which is usually associated with anophthalmos or microphthalmos, no de-



Fig. 1 (Khanna). Before operation.



Fig. 2 (Khanna). Before operation, showing further stretching than in Figure 1.



Fig. 3 (Khanna). A week after the operation

velopmental anomaly of the eye or orbit has been reported except in one case in which there was partial failure of Riolin's muscle at the points of insertion of the bands. In two other cases, though the eyes were normal, one patient had a harelip and the other a cardiac anomaly.

The pathogenesis is not very clear. The following theories have, however, been expressed but none of them is convincing:

1. Hasner attributed the condition to inflammation of the lid margins, causing defects in the epithelium which permitted mesenchyme to grow across and thus form firm strands that prevent normal separation of lids. W. F. Hardy⁹ corroborates Hasner's view.

2. Wintersteiner⁸ postulated (1908) the traumatic theory. Trauma was caused by the fingernail scratching the epithelium. There is a growth of connective tissue by mesenchymal proliferation across the line of junction at the area of the epithelial defect.

3. Judge¹⁰ believed that uniformity of the bands and their constant origin at the white line indicates "a congenital deviation" like that in coloboma, and so forth.

A brief summary of the development of the lids will help one to understand the mechanism of the anomaly. According to Mann,¹¹ in the 12-mm. stage, rudiments of lids appear from the surface ectoderm, the upper from downgrowth of the frontonasal process and the lower by upward growth of the maxillary processes. The ectoderm lining outside the lid folds becomes skin and inside changes into conjunctiva, while the rest of the lid is formed by the mesoderm. These folds grow and at 37-mm. stage, fuse together and remain so to the 160-mm. stage when they start separating again. During this period, formation of cilia, tarsal glands, and separation of Riolin's muscle from the orbicularis occur. Separation of the lids is completed by the end of the sixth month.

A study of the cases already mentioned and the cases under my observation shows that the embryonic development of the eye and its adnexa is complete and normal except for the persistence of the union of the lid margins by fibrous elastic bands. The union cannot be a simple persistence of a normal union of the lids in fetal life, since that union is purely epithelial, while here, there is abnormal subepithelial or mesoblastic growth. These bands may be abnormal conversion of epithelial adhesion into mesoblastic union; or they may be formed by abnormal subepithelial growth. This anomaly is likely to occur either at the time when the lid margins have just come together, that is at the 37-mm. stage, or sometime during the 160-mm. stage. In the former instance, besides the epithelial lining of the two lids adhering together, there is an irregular growth of the mesenchymal tissue, forming bandlike adhesions. In the later stage the anomaly may be due to abnormality in factors responsible for separation of the lids. The normal separation is probably inhibition of sebaceous secretion from glands, or cornification of the

superficial epithelium. Due to an anomaly in separation, the lid adhesions break irregularly at places and there is overgrowth of the subepithelial tissue in the form of fibrous bands.

The very fact that there is no evidence of inflammation in any part of the eye or its adnexa or in any other part of the body, makes this view highly probable. Infection of the lid margins after fusion, without affecting other parts, is also not very likely. Besides, affection of the margin would also affect the development of the lashes and tarsal glands. If infection is after fusion, it is the conjunctiva or skin which should be affected. Occurrence of intrauterine ulcerative blepharitis without affecting the development of the lid margin and leaving behind any sequela cannot be possible.

Explanation of the condition by trauma is also difficult to imagine, since trauma would hardly cause symmetric abrasions in one or both eyes that would give rise to bands which are either symmetrically situated in the two eyes or cause multiple band formations in one eye. It does not explain the hereditary or familial cases.

It is much more probable that the anomaly is due to abnormal proliferation of mesenchymal tissue at certain points on the lid margins which are covered by epithelial growth.

CONCLUSION

The history of my case shows that:

1. The condition has a familial tendency. There were only two children in the family and both were affected, though there is no history in rest of the family.
2. It has no relationship with prematurity.
3. There is no indication of trauma or inflammation as predisposing factors.
4. Its association with cleft palate and hare-lip suggest that the predisposing factor responsible for this congenital anomaly must have been present before the 10th week of intrauterine life, because the development of the face and palate and fusion of various processes occur earlier than this period.

SUMMARY

A case of ankyloblepharon filiforme adnatum is described in a family with two sisters both of whom were affected. The bands were bilateral but asymmetric. There

were cleft palate and harelip in one sister as associated congenital anomalies. This condition, in my opinion, is a congenital abnormality due to aberration of growth.

Civil Hospital.

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OPHTHALMIC MINIATURE

Ear-rings a remedy for inflammation of the eyes

A little girl of 9 or 10 months had been from birth afflicted with a purulent discharge from the conjunctive membrane of the left eye. There was a slight turgescence of the blood vessels, and the eye appeared rather sunken in the orbit. The formation of pus was so copious as to be continually running over the under lid—in all other respects the child was perfectly healthy. I had tried every remedy that my reading or observation suggested, among which were issues behind the ears, but without the least success, when then child's grandmother very *quietly* and *mildly* proposed the use of gold ear-rings. As I always entertained *as much respect* for unprofessional as professional empiricism, I determined upon employing the remedy, and accordingly inserted the rings immediately after puncturing the ears. No inflammation or apparent soreness followed the operation, and at the end of twenty-four hours there was not a vestige of the disease perceptible. Three or four weeks after this, I removed the rings; the next day the eye was full of pus. They were then replaced, and the purulent discharge ceased as before. After this they were worn constantly for seven or eight years, and without any return of the affliction.

I am aware that the *very scientific*, of our profession, sneer at these things: but with their leave, I would remind them that perhaps, *there may be* "more things in heaven and earth, than are dreamed of in their philosophy."

H,

New York, Sept. 6th, 1836.

Boston Medical & Surgical Journal, 15:110 (Sept. 23), 1836.

OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.

Abstracts of papers presented before the Midwestern Section of the Association for Research in Ophthalmology, Iowa City, March 30 and 31, 1957

HERMANN BURIAN, M.D., *Section Chairman*

THEODORE SCHLAEGEL, M.D., *Section Secretary*

Early components of corneal wound closure. James E. McDonald, M.D., University of Illinois College of Medicine, Chicago.

The purpose of this work was ascertaining the relative parts played in early components of corneal wound closure such as corneal wound swelling, retraction of Descemet's membrane, and fibrin. Central corneal incisions were made on rabbits' eyes and the course of wound closure was studied continuously under the slitlamp for a period of one hour. Histologic sections and slitlamp photographs were made.

The same procedure was repeated on newly killed animals. The differences between the closure activities in the living and dead animals were noted. The same procedure was repeated on heparinized rabbits and it was found that the fibrin paralysis so produced prevented corneal sealing of the wound. The same procedure was repeated on cats, dogs and monkey eyes, and five human eyes about to be enucleated. The course of wound closure was studied and described.

The conclusions reached were that fibrin rather than approximation of the corneal wound by swelling is the fundamental early agent of closure of corneal wounds.

Effect of occlusion of the common, external and internal carotid arteries upon the retinal arterial pressure.

Robert W. Hollenhorst, M.D., Section of Ophthalmology, Ronald E. Wilbur, M.D., Fellow in Ophthalmology, and Hendrik J. Svien, M.D., Section of Neu-

rologic Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

For diagnostic purposes, measurements of the diastolic blood pressure in the central retinal artery were made with the ophthalmodynamometer of Bailliart during compression or ligation of the exposed common, external, and internal carotid arteries. Such diagnostic measurements were made on three patients who were undergoing radical dissection of glands in the neck, on six patients who could not tolerate ligation of the internal carotid artery, on three patients who tolerated ligation of the common carotid artery, on five patients who tolerated ligation of the common carotid artery followed later by ligation of the internal carotid artery, and on eight patients who tolerated ligation of the internal carotid artery.

Although the measurements obtained from each patient were constant and closely repeatable, considerable variation in the measurements between patients was found when the identical procedures were used. Compression of the external carotid arteries caused no change in the retinal arterial pressure but there was invariably a decrease in pressure when the blood flow through either the common or internal carotid artery was compromised. We judge that the extent of this decrease in pressure is proportionate to the extent and efficacy of the extracranial and intracranial collateral channels to the internal carotid artery.

If it is found that compression of the common carotid artery or of the internal

carotid artery produces a decrease of 20 to 50 percent, or a decrease to a level of 30 to 35 mm. Hg, in the diastolic pressure of the central retinal artery, later ligation of the compressed carotid probably will be safe, and not attended by ischemic sequelae in the central nervous system. Such ligation also probably will be effective in reducing the risk of future rupture of the cerebral aneurysm.

If, however, compression causes the retinal arterial pressure to decrease to near zero, and if this level persists even after two minutes, the danger of complications is increased, and should alert the surgeon to such hazards.

Retinal artery blood pressure determinations in surgery of the carotid system.

Frederick C. Blodi, M.D., and Maurice W. Van Allen, M.D., Veterans Administration Hospital, Iowa City, Iowa.

Percutaneous digital compression of the cervical carotid system produced a significant drop on the same side in either systolic or diastolic retinal blood pressure or both in nine of 10 patients so tested and did so on either side. The percentage of blood pressure drop in the retinal arteries produced by digital compression of the cervical carotid system, when expressed as an arithmetic average was about 50 percent for both systolic and diastolic values. This percentage drop for systolic pressures is in the same range as that reported for direct pressure readings in the internal carotid artery when the common or internal carotid are occluded proximally.

Comparative retinal artery pressure studies in three cases of proven internal carotid artery occlusion revealed that pressures on the side of occlusion were lower than those on the contralateral side by 30 to 49 percent in systolic and 27 to 54 percent in diastolic readings. Two of the three cases were subjected to surgery without preliminary angiography and in

these the retinal artery pressure studies proved to have given substantial and valid support to the clinical diagnosis.

Determination of retinal artery pressures is a simple and valuable aid to diagnosis of occlusive vascular disease of the carotid system. It promises, as well, to be of value in directing the best use of angiography.

Studies of pressure in the carotid system, direct or indirect, are not as valuable as we would desire in predicting the result of proposed carotid ligation. It would seem, however, that the simple method of ophthalmodynamometry may eventually prove to yield as much practical information in this regard as direct intra-carotid pressure measurements. (Will appear in full in the *Journal of Neurosurgery*.)

The steady-state of tritium in the anterior chamber of rabbits. Max Friedman, B.S., Frank W. Newell, M.D., George V. LeRoy, M.D., and George T. Okita, Ph.D., The University of Chicago. This study was supported in part by research grant No. 105 of the Fight for Sight Grants-in-Aid of the National Council to Combat Blindness, Inc.

The steady-state rate of exchange of water between the blood plasma and the anterior chamber aqueous humor in the rabbit was studied, using tritiated water (HTO) as a tracer substance for water. A tracer dose of HTO (approximately 1.0 mc.) was injected into the peritoneal cavity of anesthetized albino rabbits and serial samples of blood withdrawn by means of a polyethylene cannula in the femoral artery. A single sample of the anterior chamber aqueous humor was obtained from each eye by paracentesis. The samples of plasma and aqueous humor were assayed in a liquid scintillation counter in a toluene system using 2,5 diphenyloxazole as the phosphor.

The steady-state rate of movement of

water between the plasma and the anterior chamber aqueous humor was estimated by solving for K_{PA} by numerical integration of the equation:

$$\frac{dC_A}{dt} = K_{PA}[C_P(t) - C_A(t)]$$

$C_A(t)$ = activity of HTO in anterior chamber aqueous humor at time t .

$C_P(t)$ = activity of HTO in plasma at time t .

K_{PA} = the fraction of aqueous humor water in the anterior chamber which exchanges with the plasma each minute.

The corresponding half-life ($T_{1/2}$) of anterior chamber aqueous humor was then determined by the formula

$$T_{1/2} = \frac{0.301}{-\log_{10}} (1 - K_{PA}).$$

The estimates for ($T_{1/2}$ on this basis were between 4 and 12.5 minutes.

The average half-life for the entire series of 23 rabbits was seven minutes which corresponds to a steady-state turnover of 9.4 percent of the anterior chamber aqueous humor each minute.

The effect of Diamox on the composition of the aqueous humor in dogs. C. S. Fan, M.D., S. T. Jones, M.D., and Peter C. Kronfeld, M.D., Illinois Eye and Ear Infirmary, University of Illinois School of Medicine, Chicago.

The original purpose of this study was to investigate, in greater detail than had been done before, the effect of anterior chamber taps upon the composition of the aqueous of the contralateral eye. The components studied were proteins, chlorides, total CO_2 and ascorbate. The aqueous specimens were obtained by needle puncture of the anterior chambers of dogs under nembutal anesthesia done at intervals ranging from one to 180 minutes.

Blood specimens were obtained at the same time from the surgically exposed femoral artery and vein. As the work progressed the potential value of deliberate changes in body fluid chemistry during the experiment became apparent and Diamox was chosen to cause such changes.

Uncomplicated needle paracenteses did not cause a change in the protein content of the contralateral eye. If the needle track became fistulous or was made so intentionally a consensual rise of the protein content occurred in the contralateral eye. This rise could be prevented by retrobulbar administration of xylocaine prior to and on the side of the first chamber tap.

In uncomplicated experiments consensual effects upon other aqueous components were not demonstrable except for ascorbate. The chlorides proved to be stable during the first two hours of the experiment and of the anesthesia and to drop three to four percent during the third hour. The total CO_2 remained unchanged during the first hour. During the second and third hour the readings were more scattered with a slight trend toward a rise. The values for ascorbate showed a significant initial difference between the right and left eye in a significant number of animals. This initial concentration difference made the evaluation of the changes occurring during the experiment somewhat uncertain, but there was an upward trend during the second and third hour. The ascorbic acid content of the plasma rose significantly in every experiment. Under the influence of Diamox the total CO_2 values in the aqueous were found to be somewhat lower, the ascorbic acid values very considerably higher. In the blood corresponding changes of lesser magnitude were observed. pH measurements with a glass electrode in aqueous, arterial and venous blood are in progress.

The results are compatible with the concept of Diamox inhibiting the rate

aqueous flow without interfering with the ascorbic acid transfer into the aqueous. Diamox highlights the unique position of ascorbate among the components of the aqueous.

Influence of vitreous volume on depth of the anterior chamber. Daniel Snyder, M.D., University of Illinois, College of Medicine, Chicago.

The influence of increased vitreous volume on the depth of the anterior chamber was studied. The investigation was carried out on rabbit eyes by measuring the depth of the anterior chamber, and then increasing the vitreous volume by approximately 15 to 20 percent by injecting 0.15 to 0.20 cc. of saline into the vitreous bowl.

The average depth of the anterior chamber of 16 rabbits initially was 2.9 mm. with a standard deviation of 0.36 mm. Immediately after the intravitreal injection, the average chamber depth was 2.7 mm. with a standard deviation of 0.538 and approximately 30 minutes after the injection in 12 eyes, the average chamber depth was 2.74 mm. with a standard deviation of 0.511 mm.

From these statistics, it can be concluded that change of vitreous volume does not influence the depth of the anterior chamber under the conditions of this experiment.

Urinary excretion of citrates in humans following administration of acetazolamide (Diamox). Anwar Shah, M.D., Marguerite A. Constant, Ph.D., and Bernard Becker, M.D., Department of Ophthalmology, Washington University School of Medicine and the Oscar Johnson Institute, Saint Louis. This investigation was supported in part by a research grant, B-621, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health

Service. The research relating to this study was also financed in part under a grant to Washington University School of Medicine made by the Alfred P. Sloan Foundation, Inc. The grant was made upon the recommendation of the Council for Research in Glaucoma and Allied Diseases. Neither the Foundation nor the Council assumes any responsibility for the published findings of this study.

Total daily excretion of urinary citrates has been studied in 10 different subjects on 24 different occasions both before and after administration of 250 mg. of acetazolamide. In each patient there was a diminution in citrate excretion with an average decrease of 61 percent \pm 13 (S.D.). The excretion of urinary citrates was even lower in patients on long-term acetazolamide therapy and less than five percent of normal in two of these individuals with recurrent ureteral colic.

In vitro lens studies: I. Technique and preliminary results of maintenance of lens culture for 24 hours. Marguerite A. Constant, Ph.D., Washington University School of Medicine, Saint Louis. (With the technical assistance of Rosalie Smith and Tommie-Ray Tracy.) This research was supported in part by the USAF under Contract No. AF 18 (600)-1269; monitored by the USAF School of Aviation Medicine, Randolph Field, Texas.

Rabbit lenses have been cultured in vitro using TC199 as the basal media and air as the gas phase. The glycolytic activity of the lens and the mitotic activity of lens epithelium have been studied during culture periods of two to 24 hours and after the addition of various compounds. Unsupplemented TC199 media maintains normal mitotic activity for approximately six hours. Supplementation of this media with tris(hydroxymethyl) aminomethane prolonged the period of

normal mitotic activity to 16 hours. The mitotic activities were checked by comparing the total mitotic cell count of the unincubated lens with that of the cultured lens and by the use of colchicine added at different time intervals. The effects of myleran, chlorambucil, alloxan, acetazolamide, sodium thiocyanate and of pH on these activities were also studied. As noted by others, the over-all glycolytic activity of the lens does not appear to correlate with the mitotic activity of the lens epithelium.

The effects of oxygen tension on the growth characteristics of human lens epithelium in culture. J. G. Mamo, M.D., and P. J. Leinfelder, M.D., Department of Ophthalmology, College of Medicine, State University of Iowa, Iowa City.

A study of the metabolism of lens epithelium was approached by using tissue culture methods. Human lens epithelium, obtained from lenses removed at cataract operations, was cultured in roller tubes. Chicken plasma was used for making a clot, and a mixture of 20-percent chick embryo extract, 40-percent horse serum, and 40-percent Tyrode's solution was used as a nutrient fluid.

Gas mixtures of 95% N_2 + 5% CO_2 , 5% O_2 + 90% N_2 + 5% CO_2 , 10% O_2 + 85% N_2 + 5% CO_2 , air, 50% O_2 + 45% N_2 + 5% CO_2 , 75% O_2 + 20% N_2 + 5% CO_2 , 95% O_2 + 5% CO_2 were used on these cultures and their effect on the growth of the epithelium was studied. Cultures with air alone were used as controls.

The gases were mixed in a spirometer, filtered through cotton, and moistened by passing through Tyrode's solution. Gassing of the cultures was done for one and a half minutes at the rate of three to four liters per minute.

The criteria used for the interpretation of the results were: arrest of growth, ac-

cumulation of fat in the cells, and disintegration of the cells.

Each experiment was repeated an average of three times.

The following results were obtained: human lens epithelium grows best under air. When 95% N_2 + 5% CO_2 was used, the culture showed inhibition of growth and some accumulation of fat. However there was no disintegration or death of cells. The cultures survived for long periods of time, and were occasionally accompanied by new growth formation.

Under 10% O_2 + 85% N_2 + 5% CO_2 , cultures showed somewhat less growth than under air, and under 5% O_2 + 90% N_2 + 5% CO_2 , the effect was even less favorable.

With the higher oxygen concentrations, 50, 75, 95 percent, early degenerative changes were noted, the amount of degeneration going parallel with the concentration of oxygen used.

Interpretation of results. In this study, human lens epithelium showed the best growth when air was used, indicating an aerobic metabolism of this portion of the lens. Survival and growth under anaerobic conditions occurs but migration and increase in the number of cells is considerably less active. Occasionally, there appears to be a period of readjustment to anaerobiasis, after which the epithelium grows well.

Between the above two, and particularly at the level of five-percent oxygen, growth was markedly inhibited. This can be explained on the possibility of a reduction of carbohydrate breakdown showing its most adverse effect at this particular oxygen concentration.

Oxygen concentrations above 20 percent proved toxic to the lens epithelium, the degree of toxicity being proportional to the oxygen concentration.

Effects of iodoacetic acid on ocular inflammatory responses. Syng-Min Hong,

M.D., Paul A. Cibis, M.D., and Marguerite A. Constant, M.D., Washington University School of Medicine, Saint Louis.

Inhibition of leukocytic infiltration into the turpentine injured cornea could be achieved in rabbits by intravenous injection of a one-percent solution of sodium iodoacetate of a pH of 7.4 in doses from 30 to 70 mg./kg. body weight.

Subconjunctival injections of a 0.1 to 1.0 percent solution of sodium iodoacetate around the limbus did not prevent the migration of leukocytes into the turpentine injured cornea.

The histologic changes following an intrastromal injection of a 0.5-percent solution of sodium iodoacetate are described and discussed. Local administration as well as systemic application of steroids did not prevent the development of the leukocytic infiltration in the turpentine injured cornea as effectively as did sodium iodoacetate.

Constant pressure tonography. Robert A. Moses, M.D., Department of Ophthalmology, Washington University School of Medicine and the Oscar Johnson Institute, Saint Louis. This investigation was supported in part by a research grant, B-621, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service. The research relating to this study was also financed in part under a grant to Washington University School of Medicine made by the Alfred P. Sloan Foundation, Inc. The grant was made upon recommendation of the Council for Research in Glaucoma and Allied Diseases. Neither the Foundation nor the Council assumes any responsibility for the published findings of this study.

Since the measurement of the coefficient of scleral rigidity (E) has been difficult and uncertain, most tonographers use

an assumed average value of E in their calculation of coefficient of facility of outflow, C . In eyes with scleral rigidity which deviates from the average value, this assumption will introduce a large error in C . Efforts must therefore be directed toward correcting for or avoiding the errors introduced by scleral rigidity variations.

If pressure in the eye during tonography (P_t) be kept constant ($P_{tav} = P_t$), the distension of the sclera will be constant and there will be no change of volume of the scleral contents ($\Delta V_s = 0$). Thus, scleral rigidity is eliminated from the volume factor and:

$$C = \frac{\Delta V_s + \Delta V_e}{(P_{tav} - P_o - \Delta P_v)t}$$

is reduced to

$$C = \frac{\Delta V_e}{(P_t - P_o - \Delta P_v)t}$$

ΔV_e = change in volume of corneal indentation

P_o = intraocular pressure in undisturbed eye

ΔP_v = change in episcleral venous pressure due to tonography = 1.5 mm. Hg

t = time in minutes

It is noted that along any isobar of the Friedenwald nomogram tonometer plunger weight is linearly proportional to scale reading. Accordingly, if weight be added to the plunger in a linear relation to the scale reading, the intraocular pressure during tonography should remain constant. In the present experiments, this has been done by beginning tonography with a standard plunger weight as is conventionally done. At a given scale reading (P_t) mercury is expelled from a syringe into a cup on the plunger in linear proportion to the scale reading in the ratio weight/scale unit required at that P_t . Intermediate plunger weight values of

V_c are obtained from the nomogram by interpolation.

In addition, by determining P_0 with the Goldmann aplanation tonometer, the scleral rigidity factor can be virtually eliminated from tonography.

The results of the application of such constant pressure tonography measurements to human eyes will be discussed.

An analysis of the illumination technique of Cibis. Robert C. Drews, M.D., Department of Ophthalmology, Washington University School of Medicine and the Oscar Johnson Institute, Saint Louis. This investigation was supported in part by a Fight for Sight Grant-in-Aid, No. 185, of the National Council to Combat Blindness, Inc., New York City, New York.

The Cibis technique of illumination for microscopy (Cibis, P. A., Microscopy with a new illumination technique. *Am. J. Ophth.*, 42:278-287, 1956.) is of especial interest to ophthalmologists because it permits visualization of zones of discontinuity in eosin-stained sections of the lens. In certain cases the technique also creates striking color and brightness differences between tissues which are almost indistinguishable when viewed with ordinary transmitted illumination. An understanding of the physical mechanisms underlying these color shifts was thought desirable.

Refraction, diffraction, interference, reflection, and polarization were found of little or no significance in color production. The darkfield produced is essential for the visibility of surface details, eosin fluorescence effects, and scattering. Eosin absorption and fluorescence characteristics account for most of the color changes seen. The zones of discontinuity of the lens are appreciated with Cibis illumination because they contain many minute granules which scatter the oblique light. This scattering locally obliterates the darkfield.

Studies of the corneoretinal potential. Carl Keller, B.A., and Frank W. Newell, M.D., The University of Chicago. This study was supported in part by research grant No. B-802 of the United States Public Health Service.

Marg (*Arch. Ophth.*, 45:169, 1951) indicated that electro-oculography is an accurate, objective method for recording eye movements. François, et al. (*Brit. J. Ophth.*, 39:398, 1955) "... recommended that the electro-oculography could be used clinically in testing the motility of the eyes or as a functional test of the retina. ..." The literature on the corneoretinal potential is reviewed with respect to the source of the potential, experimental alterations in the potential, recording eye movements and its use as a functional test of the retina.

Subjects alternately fixed black spots on a white chart or small red electric bulbs (GE 1449R) 113 cm. from the cornea. A movement from the center to five degrees to the same side as the eye was used as the standard movement. The potential was also measured during dark adaptation using the same movement. Pontocaine was used as a local anesthetic. The potential was picked up by a mosquito clamp electrode fastened at the outer canthus and resting on the globe and referred to an indifferent electrode—a 27-gauge needle in the midline of the scalp. A Gilson electroencephalograph was used to record the potentials.

RESULTS

| | | |
|----|---|--------------|
| 49 | normal eyes | 415 ± 290 μv |
| 19 | normal O.D. | 470 ± 125 μv |
| 30 | normal O.S. | 380 ± 210 μv |
| 14 | normal eyes with normal opposite eyes | 420 ± 315 μv |
| 20 | normal eyes with pathological opposite eyes | 410 ± 260 μv |
| 38 | pathologic eyes | 450 ± 295 μv |
| 21 | pathologic O.D. | 440 ± 250 μv |
| 17 | pathologic O.S. | 465 ± 365 μv |

The diseased eyes include retrobulbar neuritis, optic atrophy, retinal detachment, retinitis pigmentosa, chorioretinitis, uveitis, iritis, glaucoma and senile cata-

tracts. There were no blind eyes in this group. All of these had electro-oculographic values well within the normal range.* Nine normal eyes showed a 45 ± 18 percent drop in the electro-oculogram during dark adaptation. Twenty pathologic eyes showed a 45 ± 21 percent drop. All of the decreases in the pathologic eyes were well within the normal range.

Our measurements disclose that the corneoretinal potential probably has a higher average value than previously reported. We found the normal range of potential to be quite large. The electro-oculogram of the pathologic eyes we measured could not be distinguished from the electro-oculogram of normal eyes. Dark adaptation had the same effect on the electro-oculogram of normal and of diseased eyes.

The average standard deviation for 10 consecutive movements was 15 percent. When both the vertical and horizontal components of eye movements were recorded simultaneously by placing one electrode at the outer canthus and one on the lower lid, purely horizontal movements produced potentials indicating appreciable vertical movement and vice versa. Therefore, even if a subject were calibrated immediately before recording his spontaneous movements, the record of his spontaneous movements would have an error of at least 15 percent and could even be qualitatively inaccurate, that is, indicating a horizontal movement where the real movement was purely vertical. We must conclude that this method cannot be depended upon to record eye movements precisely. Because the corneoretinal potential has a wide normal range, it is not a useful test of the health of the retina.

Enzymology of the refractory media. E.

Albert Zeller, M.D., Department of Biochemistry, Northwestern University Medical School, Chicago.

The description of any biologic phe-

nomenon is complete only with the inclusion of the enzymes, even if these happen to play a minor role in a given event. Therefore, in order to gain a thorough knowledge of the materials—their formation, maintenance, specific function, breakdown and other pathologic changes—which make up the realm of the refractory media, their enzymic apparatus has to be investigated. On the other hand, in analyzing these systems, which promise to be more simple than others, much needed information about the interrelationships of enzymes may be obtained.

While a considerable number of enzymologic studies with lenticular extracts have been carried out little is known about the enzymic systems of the corpus vitreum. If we disregard the interesting observations made in 1922 by G. LoCascio, which should be checked with modern procedures, only few determinations on esterases and carbonic acid ox anhydrase are found in the literature. To this short list data on ATP-ase, cholinesterases, ali-esterase, (exo-)peptidases, endopeptidases (kathepsins), catalase, and pyrophosphatase have been presented by this laboratory. With the exception of the last three enzymes, modern analytic methods revealed measurable and reproducible activities. Naturally, in a medium which contains 98-percent water, not very high *Q*-values can be expected. However, when the calculations are based on the protein content rather than on the fresh tissue weight, rather high activities are obtained. While no doubt is left about the conclusion, that the corpus vitreum is endowed with a set of enzymes, most questions about the origin and the function of these remain still to be answered.

The formation of a cataract is accompanied by physicochemical changes of the lenticular proteins. It is assumed, but not proven, that these proteins like those of other mammalian tissues are in a dynamic equilibrium. By this it is meant that the

lenticular proteins are being constantly degraded and resynthesized at a rate characteristic for each. "While the synthetic mechanism received constantly growing attention, the nature of the equally relevant and possibly related mechanism of degradation has received little attention." In trying to fill out this gap, the kathepsins of the refractory media were studied. While A. C. Krause's autolysis experiments indicated the occurrence of proteinases in the lens, no direct measurements of proteolytic activities have been undertaken before. With the help of sensitive manometric methods, which were partly developed in this laboratory, the presence of a chymotrypsin-like and small trypsinlike activities were observed in lenticular extracts of various species. The Q-value of cataractous lenses (rabbit, man) for the chymotrypsinase is strongly reduced. The same is true for two peptidases which catalyse the hydrolysis of glycyl-L-leucine and L-leucylglycine. Preliminary results indicate that the glycyl-L-leucine attacking peptidase is depressed in the corpus vitreum of rabbit eyes which have been irradiated with X rays. The biologic and pathologic roles of these enzymic changes require further investigation.

Form and brightness discriminations and their interocular transfer in relation to early visual experience. Austin H. Riesen, Ph.D., Department of Psychology, and K. L. Chow, Ph.D., Department of Physiology, The University of Chicago.

Visual science has known for many years that the two eyes are not in all individuals equivalent for the perceiving or discriminating functions. Where ocular defect is ruled out and a central lack of equivalence is implicated, the term amblyopia ex anopsia is appropriate for certain clinical manifestations. Animal experiments reveal another type of central independence, usually referred to as

a lack of interocular transfer. The exact relationship between these various anomalies of the perceptive functions is not yet understood.

Previous work has shown that at least two different experimental procedures can produce animal subjects whose vision from each eye is behaviorally independent. One of these is through surgical interference with the interconnections between the cortical areas receiving input from each eye. The other is through control of the kinds of visual stimuli to which the animals are exposed, either monocularly or binocularly, during the early postnatal weeks or months. Our work at Chicago and at the Yerkes Laboratories of Primate Biology has demonstrated a number of different and independent effects of selective visual restriction. With primates and cats we find that specific kinds of discriminative abilities may be separately learned through one or the other eye in a given individual. Under sufficiently varied environmental conditions the organism develops a high degree of ocular equivalence (interocular transfer). Control of the visual environment can produce a selective equivalence. For example, we have exposed kittens to diffuse unpatterned light during early weeks of life. These then show equivalence for brightness discriminations learned monocularly, but lack of equivalence for form. Furthermore, such kittens learn brightness habits quickly and learn initial form or visual movement discriminations only with great difficulty.

The simultaneous exposure of both eyes to visual patterns is the most effective environmental procedure for insuring the development of a high degree of interocular transfer. Equivalence of the two eyes is less if the eyes are alternately exposed, but this is a sufficient condition for transfer of discrimination habits when the patterns to be discriminated are quite different. If one or both eyes are exposed only to diffuse light from birth the first

form discrimination learned with either eye fails to appear when the second eye is exposed.

The phosphene of quick eye motion. Bernard R. Nebel, Ph.D., Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Illinois.

Eye movement phosphenes of a hitherto incompletely recorded but probably common type are described. Seven persons out of about 100, now all over 40 years of age, reported consistent and repeatable observations. The flick phosphene is ascribed to an instantaneous and transient deformation of the posterior surface of the vitreous emanating in a particular "polarized" pattern from its attachment at the optic disc. This deformation is due to an inertial lag of the vitreous when the eye is suddenly "flicked." The deformation is postulated to be directly transmitted to the retina and to cause, in the deformed regions on the retina, previsual activity which is observed entoptically as the flick phosphene in the dark-adapted and rested eye. The phenomenon is considered to be possibly an early senescent sign of a normal, slight shrinkage of the vitreous. This prerequisite condition differs from frank vitreous detachment, although the flick phosphene may be related to Moore's "lightning streaks." As a subclinical phenomenon, the flick phosphene may have potential diagnostic and prognostic value.

Changes in the tonogram during accommodation and during relaxation. Mansour F. Armaly, M.D., and Hermann M. Burian, M.D., Department of Ophthalmology, College of Medicine, State University of Iowa, Iowa City.

The purpose of this study is to investigate the influence of accommodation on the facility of outflow, C, of aqueous humor as estimated by tonography.

To stimulate and control accommoda-

tion and relaxation, an apparatus was designed through which a Landolt C could be presented to the subject at a distance of 25 cm. from the eye, with and without a +4.0D. add. The size of the target was sufficiently small that only young persons with 6/6 vision or better could comfortably maintain seeing it for four minutes. The fact that the subject was seeing was checked by having him indicate with the index finger the direction of the opening which was changed randomly at a rate of 20-50 times/minute, both during accommodation and relaxation. The whole apparatus could be rotated during accommodation so that the angle of associated convergence was completely taken up by the seeing eye, thus keeping the eye on which tonography was to be performed in a vertical position both during accommodation and relaxation. All tonographic records of one subject were obtained from the same eye keeping the other as the seeing eye throughout the study. Nothing by mouth was allowed for at least one hour before the test.

The test consisted of two tonograms, one during accommodation and the other during relaxation. Replication was achieved by reversing the sequence of accommodation and relaxation in each test in order to eliminate and evaluate the effect of the order in which they came. A steady-state was considered achieved if the eye recovered a pressure within ± 0.4 scale reading of that at the beginning of the first tonogram, and if this did not change more than 0.4 scale units when three determinations were done over a period of two minutes.

Seven young students were selected from a group of 13 who volunteered for this study. The basis for rejection was inability to see the target comfortably under the conditions of the experiment. A complete examination of their eyes was done and their refractive error determined and corrected. Gonioscopy revealed no significant difference in the appearance of

their angles. A minimum of 24 hours existed between successive tests.

Ninety-four tonograms were obtained and values for P_o and C were derived from the tables based on the 1955 nomogram of Friedenwald.

A one-percent level of significance was chosen to evaluate variance. The following were the results of the statistical analysis:

1. C values during accommodation were significantly larger than those during relaxation; the significance was very high at the one-percent level.

2. This effect was present irrespective of whether accommodation preceded or followed relaxation in the test.

3. The response of these subjects differed significantly from subject to subject.

Similar results were obtained from the analysis of variance on F values as it is to be expected, since P_o was not significantly different in the two situations.

The conclusions drawn from this study is that tonography performed during "effortless" accommodation gave C values that are significantly larger than those obtained during relaxation. Whether this represents a real increase in facility or merely an apparent one due to an increase in ocular rigidity during accommodation we are not yet in a position to tell. The reason for bringing up this point stems from other studies to be reported which seem to show that the ocular rigidity coefficient can be significantly influenced by extraocular orbital factors. Our attempt to evaluate this factor in these situations with the 5.5- and 10-gm. weight was not successful because of the very wide range of variations and of the high frequency of meaningless results for P_o if we adhered to the 1954 nomogram. We have recently acquired the 1955 nomogram and hope it will aid in providing the desired information to help rule out the possible effect of ocular rigidity.

Accommodation-convergence association:

Experiments with neosynephrine, pilocarpine, and physostigmine. Fred C. Sabin, M.D., and Kenneth N. Ogle, Ph.D., Mayo Clinic, Rochester, Minnesota.

In a recently published paper data were described which showed that the accommodative convergence to accommodation [(AC)/A] ratio was markedly elevated by the cycloplegic action of homatropine. The present study concerns the effect of mydriasis without cycloplegia (neosynephrine) and miosis with cyclodiamia (pilocarpine 2.0% and physostigmine 0.25%) on the (AC)/A ratio. Ten young nonpresbyopic individuals served as subjects. A study of the results showed that not only a large pupil without cycloplegia, but even miosis with cyclodiamia did not alter significantly the (AC)/A ratio. Of interest was that in all subjects the pilocarpine and physostigmine caused a shift of the horizontal phorias in the exophoric direction. The results are discussed with reference to the mode of action of the drugs and of the relationship of the small pupil to the stimulus to accommodation.

On the accommodative convergence and the proximal convergence. Kenneth N. Ogle, Ph.D., Section of Biophysics and Biophysical Research, and Theodore G. Martens, M.D., Section of Ophthalmology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. (The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.)

The accommodative convergence-accommodation ratios and the proximal convergence ratios were determined, first, for 28 subjects by the phoria technique, and second, for 104 subjects, for the most part clinical patients, using the fixation-disparity technique, which was believed to give more stable data, since the test requires fusion and both eyes are subject

to the same stimulus to accommodation. The data suggest that if the accommodative convergence is to be determined by measuring the phoria at near visual distance with only a few measurements, minus lenses would probably lead to less error than plus lenses.

The (A-C)/A ratios were essentially the same from the two methods, the mean being $3.5\Delta/D$ with a standard deviation of $1.2\Delta/D$. The mean proximal convergence ratio was different, being $0.9\Delta/D$ (S.D. = $0.9\Delta/D$) from the phoria technique, and $1.5\Delta/D$ (S.D. = $1.62\Delta/D$) from the fixation-disparity technique. The distribution of the proximal convergence ratios for the 104 subjects seemed to be normal, and 16 percent of the ratios were negative.

The association of the proximal convergence with dioptric change in the distance of the test object was shown to be linear, as was also that of the accommodative convergence with change in the stimulus to accommodation. To what extent the difference between the proximal convergence ratios measured by the two methods is significant is not clear, but the difference in selection of the two groups of subjects and in the conditions of the tests is emphasized. More weight is attached to the proximal convergence measured by the fixation-disparity technique than to that measured by the phoria technique.

The role of the sympathetics in visual accommodation. David G. Fleming, Ph.D., Physiology Department, University of Kansas, Lawrence.

The role of the sympathetic portion of the autonomic nervous system in distance accommodation is currently being investigated. The hypothesis that the sympathetic exerts its effect by regulating the caliber of the arterioles in the ciliary body is being evaluated in the rabbit. On the basis of such a mechanism, changes in vessel diameter would alter the blood

volume and therefore the size of the ciliary body and, in this manner, the tension exerted by the zonule on the lens.

Since direct blood volume or flow measurements within the ciliary body are not as yet possible, indirect techniques have been employed. Refractive changes in the rabbit's eye as determined by retinoscopy have been compared with blood flow through the ear. Thermistors were used to measure ear temperature which was the index for blood flow.

It was possible to demonstrate unilateral vasoconstriction and increased hyperopia as a result of unilateral stimulation of the cervical sympathetic nerve.

Second, unilateral extirpation of the superior cervical ganglion brought about a relative myopia in the eye on the operated side of 1.8D. and an increase in ear temperature of over 2.5°C . Within three days ear temperature and refractive power returned to preoperative values.

Fundus photographs were taken daily in the immediate pre- and postoperative periods. They revealed no discernible changes in the retinal vascular bed.

A third set of experiments compared refractive changes with intraocular pressure changes resulting from supracervical gangliectomy. Direct manometry with a fine-gauge needle and a Statham transducer was used to measure intraocular pressure.

A strong time correlation between the increase in accommodation and the fall in intraocular pressure was noted. On the first postoperative day the intraocular pressure was 8.0 mm. Hg; by the third postoperative day it was back to its normal value of 22 mm. Hg. Extirpation of the superior cervical ganglion brings about a transient change in the dynamic equilibrium of the eye as evidenced by a drop in intraocular pressure and decreased zonular tension, and these changes may be correlated with blood flow changes in the ear.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

432nd Meeting

November 21, 1956

DR. EDWARD A. CRAMTON, *presiding*

CASE PRESENTATIONS

CASE 1: OPTIC NEURITIS

DR. JOSEPH L. DOWLING presented a nine-year-old boy who was admitted to the hospital on August 21, 1956. Two or three weeks prior to his admission he had noticed a marked diminution of vision in his right eye. There was no antecedent history of ocular disease or trauma. However, the boy had received his second poliomyelitis vaccine injection two days before the onset of his visual difficulty.

Examination at the time of admission showed the vision in the right eye to be 3/300. The right fundus showed a marked elevation of the optic nerve with obliteration of the normal contours. The entire retina was extremely edematous with marked congestion of the veins and a marked exudation throughout extending well into the periphery. All observers at this time agreed he had an occlusion of the central retinal veins. It was felt that the primary pathologic process was an optic neuritis as manifested by this severe papillitis. One or two observers suggested the possibility of an atypical Coats' disease.

After an extensive workup in the hospital, the only thing that was really impressive was the possibility as to whether or not this might be an adverse reaction to poliomyelitis vaccine—something that had not been reported before. Dr. John Enders was contacted and he said he doubted very much if this could be so.

We are presenting the case for two reasons: (1) to see if any one has any idea what this lesion might represent and (2) to find out if any one here has seen any ocular reaction to poliomyelitis vaccine.

The boy's left eye has been normal throughout with 20/20 vision. At present the vision in his right eye is 20/200. There has been quite a change in his fundus since he was first seen. It is apparent now that he did not have an occlusion of the central retinal vein.

Discussion. The consensus was that this was a possible case of atypical Coats' disease. None of the members reported any adverse ocular effects from poliomyelitis vaccine.

CASE 2: SPASM OF THE NEAR REFLEX

DR. IRVIN S. TAYLOR presented a 45-year-old woman who had a long history of neurosis and all sorts of hysterical complaints. She had been in and out of the hospital many times. At present she is in the hospital because of a hysterical dysphonia of long standing. She is also suffering from malnutrition. The doctors have judged her a self-made invalid.

When the patient was seen by the ophthalmologist she had two complaints: "Dr., I want some reading glasses; and Dr., for years when I look to the side my eyes cross or when I look up my eyes cross."

This was a very good description of her ocular condition, for when she looked to the side or when she looked up she had a convergence spasm. On lateral gaze or upward gaze or on any manipulation about the eyes she had this tremendous spasm which was actually painful to her. This condition has been termed the spasm of the near reflex.*

*Cogan, D. G. and Freese, C. G.: Spasm of the near reflex. *Arch. Ophth.* 54:752-759 (Nov.) 1955.

We put minus-one spheres on this woman and after she wore them for 10 to 15 minutes the spasm on horizontal gaze was eliminated. However, on upward gaze the spasm remained unchanged. Unfortunately she is hyperopic. The patient's eyes are otherwise normal.

Discussion. DR. DAVID G. COGAN: Spasm of the near reflex is not a rare entity. If you give these patients minus lenses this often corrects the spasm. This is something of a "cure." When the period of tension in the patient's life passes, the glasses can be put aside and the eyes are normal. The only other alternative is a period of psychiatric evaluation which is often not as effective as the minus glasses. It is somewhat paradoxical that minus lenses should relieve a convergent strabismus. Plus glasses often make the spasm worse.

CASE 3: FAMILIAL CORNEAL LESION

DR. BRENDAN D. LEAHEY: I would like to present this family with a very interesting hereditary defect—leukoma of the cornea, a male sex-linked hereditary defect similar to hemophilia. We have seen four cases in two different generations in four different branches of the family.

The two babies shown here have bilateral microphthalmos with marked corneal scarring and many anterior synechias. The fundus of the eyes cannot be seen. One patient who has been examined quite thoroughly apparently has no cataracts. The other two cases in the family (not shown) have microphthalmos and corneal scarring. Two of these eyes had an anterior staphyloma so extreme that enucleation in infancy was necessary.

The number of cases involved is too small to make the inheritance pattern 100 percent positive, but this is definitely a male sex-linked inheritance. The genealogic table shows that transmission is from an affected father through his daughters who are all carriers and that none of his sons have the

disease. If one of the daughters marries a normal man, then half her children will be affected. That is, half her boys will have the disease clinically and half her girls will be carriers. Because of this it appears only in boys and appears only every second generation.

Because this condition shows some variation in this family, some with different types of corneal scarring and synechias, some with microphthalmos, and some with staphyloma, it is obvious that the hereditary defect is not the corneal leukoma but rather some type of early developmental defect. This may have been brought about by some defect in the genes which cause a very early developmental defect, perhaps in the third month, and perhaps then the eyes had anterior synechias and perhaps glaucoma. In other words they inherited a defect that took different forms.

On one of the children shown here we plan to do an optical iridectomy. The other child we have studied rather carefully and we have decided not to do an optical iridectomy, as there is enough sight in one of its eyes for general visual purposes.

SCIENTIFIC SESSION

DFP IN ACCOMMODATIVE STRABISMUS

DR. S. J. BULLINGTON, Boston, Massachusetts: My interest in an evaluation of the use of DFP in the treatment of accommodative strabismus was to determine whether the binocular skills of the patient could be improved with a powerful long-acting drug. I was interested in whether this miotic drug would actually demonstrate any advantage over the conventional methods of treatment.

The series of 20 cases conformed to the classical concept of accommodative strabismus. No child under the age of six years was chosen. No child was included who had less than 20/30 vision with glasses following the use of DFP. No child whose hyperopia was greater than four diopters was included. No patient with an amblyopia was ordinarily

accepted. In all the selected cases, the eyes were straight with glasses at distance and near.

The tests of binocular function employed for each examination were: (1) The cover-uncover test while the patient was reading the smallest discernible print at distance and at near, (2) the screen and prism test at distance and at near for the patient accommodated on 20/30 test type, (3) the two-pencil test for stereopsis as is commonly used for simple convergence exercises, (4) the Verhoeff stereopter at one meter, (5) the bar-reading test.

Before the administration of DFP each patient was subjected to each of these tests with and without glasses. They were given 0.05-percent DFP in oil, one drop in each eye. One drop was used in each eye daily for one week followed by a complete examination. After this the drops were used three times a week, twice a week, or in some cases once a week depending on the therapeutic effect.

In all cases with one exception in which DFP was instilled, it was observed that within one-half hour the glasses could be dispensed with and the eyes appeared to be cosmetically straight. With the cover-uncover test the squint could often be elicited by having the patients exert maximum accommodation. In one case the squint increased following the use of DFP but in two days the patient's eyes were cosmetically straight. During the first three or four days of DFP therapy, some of the patients developed slight redness of the conjunctiva, transient headaches, and transient blurring of vision. After this period the drops caused no side effects. In no case did a sensitivity to DFP develop. In many of the cases, iris cysts were observed after one week's use of DFP. These would vary in size from one examination to the next but did not reach sufficient size to interfere with visual acuity.

On examination each of the patients had visual acuity equal to that obtainable with glasses both for distance and near. No pseu-

domyopia was reported. The residual hypermetropia was not decreased more than two diopters. Not one patient who was examined during what we considered the significant treatment period was able to perform any of the tests for binocular skills in a satisfactory manner. In fact in many of the cases the ability to perform the test was decreased. The eyes of 100 percent of the patients looked cosmetically straight even to a so-called critical observer.

My study led me to conclude, therefore, that DFP demonstrated no superiority over glasses in the treatment of accommodative strabismus except for its possible cosmetic advantages. It did not increase the ability to perform binocular skills. The possible pathologic changes which may occur in the eye would preclude its use in most cases of squint except in those very special cases in which the cosmetic advantage is of singular importance.

Discussion. DR. F. H. VERHOEFF stated that a good many years ago it seemed to him ridiculous that no one had tried miotics for accommodative strabismus. At that time there was no DFP so he used pilocarpine. He satisfied himself that the results were not any better and in fact were less satisfactory than using glasses. He did not publish his results.

DR. ALBERT E. SLOANE said he had used DFP for almost three years in private practice in cases of accommodative estropia and had found it a useful drug of extremely limited value. It is not entirely safe and must be watched continually. He has made it a general policy to increase gradually the intervals between the use of the drops. If he found that DFP kept the eyes straight but had to be maintained at regular dosage periods, for example, every three days, he went back to glasses and omitted the drug except for special occasions. The strongest dosage used was 0.05 percent. The weakest that gave results was 0.025 percent. He believed that the drug had a certain amount of value but should not be used as a permanent

substitute for glasses; rather as a method of treatment or as a temporary expedient for the cosmetic effect.

INTRASCLERAL NERVE LOOP: ITS ANATOMIC CHARACTERISTICS AND ITS CLINICAL SIGNIFICANCE.

DR. DEWEY KATZ, Hartford, Connecticut, will publish this paper elsewhere in the near future.

DIFFERENCE BETWEEN DISTANCE AND NEAR FIXATION MEASUREMENTS IN STRABISMUS

DR. MARSHALL M. PARKS, Washington, D.C.: The difference between distance and near fixation prism and alternate cover measurements are attributed to an imperfect near reflex. Those portions of the near reflex that are at fault in causing this difference are: (1) the accommodation and (2) accommodative convergence innervation. The association of innervation that serves these two phenomena is not perfect and the result is that the eyes are either overconverged or underconverged at near fixation as compared to their alignment at distance fixation. Minor differences between distance and near are usually compensated for by the fusional vergences. The near reflex was considered abnormal if the difference between distance and near was greater than 10 prism diopters.

Among 1,249 comitant esotropes and exotropes there were 50 percent with abnormal near reflexes. All the esotropes and 87 percent of the exotropes with abnormal near reflexes were more convergent at near than at distance. If the esotropia was congenital, only 16 percent had an abnormal near reflex, but in 57 percent of the acquired esotropes, the near reflex was abnormal. This fact, plus the observation that among the acquired group the average hypermetropia was plus 2.25 if the near reflex was abnormal and plus 4.75 if normal, led to the conclusion that the abnormal near reflex was an equally important etiologic factor with hypermetropia in acquired esotropia.

Fifty-one percent of the exotropes with

less "exo" at near than distance, that have abnormal near reflexes may have, in the majority of instances, developed such a reflex to assist in overcoming the "exo." Therefore, the abnormal reflex was considered to be secondary to the malalignment when complicating exotropia, but it was felt to be the primary etiologic factor when encountered among the acquired esotropes having small hypermetropic refractive errors.

Time seems to be on the side of spontaneous improvement of the abnormal near reflex in either esotropia or exotropia. Bifocals and DFP mask the abnormal near reflex in esotropia but by different approaches. Dissociation exercises (orthoptics) increase the specific fusional vergence needed to compensate for the "eso" and "exo" alignment but actually change the abnormal reflex in esotropia or exotropia little, if any. A routine of gradually diminishing strengths of DFP tends to increase the fusional vergence in esotropes; the effect is similar to that of dissociation exercises but perhaps not quite so good. Surgery directly improves the abnormal near reflex in esotropia and indirectly improves it in exotropia by doing away with the need of the compensatory abnormal near reflex.

In spite of the fact that statistics seem to suggest surgery as the treatment of choice for abnormal near reflexes, it is seldom permissible solely for the purpose of normalizing the reflex. Surgery is justified only to correct the tropia measured at distance fixation while not accommodating. It is an accident that surgery for horizontal heterotropia almost never increases the difference between distance and near prism and alternate cover measurements. It is not the design of surgery to eradicate or improve the abnormal near reflex but fortunately this most often happens. Surgery lessened the difference between the distance and near measurements in 78 percent of 143 esotropes and 90 percent of 111 exotropes.

Charles Snyder,
Recorder

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DR. BERNARD KRONENBERG, *president*

SYMPOSIUM ON RETINAL DETACHMENT

I. DIAGNOSIS AND PROGNOSIS.

DR. ROBERT J. BROCKHURST, (Boston, Massachusetts) said that detachment of the retina should be suspected whenever there is a history of light flashes, sudden onset of floaters, sudden loss of field or central vision, and trauma. The examination of the patient should include careful studies of the field of vision, biomicroscopy of the anterior segment and vitreous, and ophthalmoscopy.

Modern indirect ophthalmoscopy has several advantages over direct ophthalmoscopy in the study of retinal detachment cases. These are: (1) A larger field of view, approximately 10 times the area seen by direct ophthalmoscopy, (2) more intense illumination, (3) a binocular stereoscopic image of the fundus, and (4) visibility of the extreme fundus periphery by means of scleral depression.

The discovery of retinal breaks is of paramount importance in planning an operation for retinal detachment. Breaks which are posterior to the equator are generally easy to locate. Horseshoe tears and round tears with opercula in the vitreous are often found in the equatorial region. In addition this is a common location for holes which have developed in areas of degeneration of the retina; scleral depression often aids in the diagnosis of such holes.

Generally it is necessary to use scleral depression to locate breaks at or near the ora serrata region. Such breaks may be the result of rupture of cysts (holes), or may be associated with meridional folds (tears), or may consist of dialyses along the ora serrata itself.

The macula itself may be subject to the formation of breaks, and the use of the bio-

microscope with Hruby or contact lens is recommended in order to differentiate a true break from a cyst.

Early diagnosis of retinal detachment will lead to a higher percentage of successful operations. The finding of a vitreous hemorrhage should provoke a diligent search for a retinal break. Examination of the apparently normal fellow eye will often reveal retinal breaks and possibly subclinical detachment.

The differential diagnosis should include such conditions as retrolental fibroplasia, retinitis proliferans, Eales' disease, uveitis, choroidal detachment, old vitreous hemorrhage, exudative retinopathy of Coats, toxemia of pregnancy, angiomas of retinae, retinoschisis, and choroidal tumor.

In regard to the prognosis in a given case of retinal detachment, it is necessary to consider two factors: The prognosis for reattachment; (2) the prognosis for visual acuity.

In general the prognosis for the reattachment becomes less with detachments of longer standing. The duration of the detachment may be known by history, but in many cases this fact is hard to establish. Demarcation lines may be present, each line indicating the detachment to have been present for at least three months. The extent of the detachment also is inversely proportional to the prognosis, although by no means should total detachments be considered inoperable.

Large retinal breaks are harder to close than small breaks and thus should be assessed in arriving at a prognosis. Breaks which are located in the posterior fundus are more difficult to treat due to technical problems. The greater the number of breaks, the less is the chance that all will be closed.

Vitreous hemorrhage makes ophthalmoscopy difficult, and in some cases results in vitreous traction on the retina. Moreover, opacities in the cornea and lens and nystagmus are obstacles to fundus examination. All of these factors will lower the prognosis for reattachment.

Associated ocular disorders such as uveitis and glaucoma will complicate the retinal detachment case and allowance must be made for these conditions. Aphakia generally should not affect the prognosis unless vitreous was lost at the time of cataract surgery, or lens remnants are present which interfere with ophthalmoscopy.

The most important factor which decreases the chances for reattachment is that of vitreous traction. This is recognized by the presence of star-shaped folds, equatorial folds, large fixed folds, and breaks with rolled up edges.

Finally the condition of the sclera must be considered. Thin staphylomatous scleras may be perforated at the time of surgery, and make the placement of sutures hazardous. Sclera which is necrotic from previous diathermy is extremely easy to perforate.

In regard to the second factor, that of central visual acuity, the following conditions will lower the ultimate prognosis: duration of macular detachment; signs of vitreous traction at the macula such as star-shaped folds; degenerative changes in the macula such as cysts, breaks, and pigment; and hemorrhage in the macular area.

II. TREATMENT

DR. I. D. OKAMURA (Boston) said that the objective of any surgical treatment of retinal detachment is to close off all the retinal breaks, as stated by Gonin. Therefore, whatever the method employed, accurate localization of all retinal breaks is essential.

Until 1952, our operation of choice was retinopexy. Surface diathermy was applied and only one or two perforations were made for the release of subretinal fluid. This operation was successful in the majority of cases. The failures apparently were due to the fact that the retina would not flatten against the choroid. The logical solution in such cases was to push the choroid against the retina. For this purpose, the scleral buckling procedure was developed. This dif-

fered from the usual lamellar resection in that the location of the breaks determined the area to be resected. Generally, the buckle was placed either at the equator or posterior to it. At first the scleral buckling procedure (with excision; without a tube) was used only on unfavorable cases, such as aphakic detachments. Later this procedure was used more and more as a primary operation.

In the course of a year or so, it was noted that some of the failures with this operation were due to a buckle which was not sufficiently elevated. Dr. Schepens decided that it was necessary to place something under the mattress sutures in order to obtain a higher buckle. Polyethylene tubing was selected for this purpose. The buckle, with the addition of the tube, was now higher, smoother, and more permanent.

More difficult cases were being reattached, but there were still cases, such as those with massive vitreous retraction, which required a higher buckle than that which could be obtained in this fashion. The next step was the use of a circling polyethylene tube containing a 2-0 braided, black silk suture in its lumen. Resection was done from one half to three quarters the circumference of the globe. With a circling tube, an extremely high, permanent buckle could be obtained and, in addition, the height of the buckle could be increased by shortening the length of the tube.

One desirable byproduct of this procedure has been the shortening of the period of bed rest. Preoperatively, bedrest is not employed. Postoperatively, the patient is allowed to be up on the first to the third day. At the present time, the scleral buckling operation with a circling tube is our operation of choice.

The various operations used by us at one time or another are:

- A. Retinopexy
- B. Scleral buckling
 - 1. Without excision; without tube
 - 2. Without excision; with tube
 - 3. With excision; without tube

4. With excision; with tube
5. With excision; with circling tube

In addition to the usual instruments and materials, the following are used:

1. Desmarres corneal scarifier (Grieshaber)
2. Amsler marker
3. Polyethylene tubing, 1.27 mm. in diameter (Clay-Adams PE 90)
4. 4-0 braided, black-silk sutures on Grieshaber 82/7 needles to use on the sclera.
5. 2-0 braided, black-silk suture, to be threaded through the polyethylene tube

III. COMPLICATIONS AND RESULTS

DR. C. L. SCHEPENS (Boston) stated that complications in operations performed to reattach the retina may occur either during or after surgery. During a scleral buckling the following special difficulties may be encountered: (1) One or more vortex veins may be in the area selected for the buckling; (2) the sclera may be too weak to support the mattress sutures. Methods of handling these two problems are described. The sclera may be accidentally perforated during the placement of the mattress sutures. If the suture either causes bleeding or perforates the retina, it should be removed. If it only causes a loss of subretinal fluid, it may be left in place, provided certain precautions are taken. The procedure used to repair an accidental rupture of the sclera, during operation, is described. Intraocular hemorrhage may result either from damaging a choroidal vessel, with a suture or with a diathermy needle, or from a sudden lowering of the intraocular pressure.

Some of the postoperative complications were discussed. The silk mattress sutures may erode through the conjunctiva, particularly when they have not been adequately covered by Tenon's capsule. The same cause may produce conjunctival granulomas. When a noncircling tube is used, one of the end sutures may give way and the extremity of the tube may protrude under the conjunctiva. When removing an exposed suture, care

should be taken not to sever the 2-0 black silk which is passed through the lumen of a circling tube. One should also avoid pulling on a protruding tube unless it is certain that the tube is not anchored to the sclera.

Choroidal detachment is frequent in all types of detachment surgery. It should not be tapped unless it reaches the posterior pole. Late intraocular hemorrhage may occur either in the choroid or in the ciliary body. In the latter case glaucoma often results, with fibrin or blood in the anterior chamber, posterior synechias, atrophy of a sector of the iris, and posterior cortical opacities. Of about 2,000 cases of scleral buckling, there has been no case of established sympathetic ophthalmia. In three instances, however, this condition has been suspected.

Glaucoma may occur postoperatively, particularly in successfully treated, long-standing detachments, and in eyes which have been submitted to repeated operations.

The general impressions from about 2,000 scleral bucklings are the following: (1) As a rule no preoperative bedrest is necessary; (2) the patient may get out of bed in one to three days after operation; (3) pinhole glasses are of no benefit; (4) the patient returns to work sooner than after retinopexy; (5) recurrences are fewer and easier to reoperate.

The use of buckling procedures has improved considerably the prognosis in bad cases, such as total retinal detachments and detachments in aphakic eyes. In a number of cases where the chances of reattachment used to be 10 percent or less with a retinopexy procedure, the chances now are 50 to 60 percent. This category includes cases with marked fixed folds, with retinitis proliferans, with massive vitreous retraction, eyes which have been operated upon several times without success, and detachments which have been present for over two years. In certain cases with giant tears, however, buckling procedures have proved of no more assistance than retinopexy.

Discussion. DR. ESTERMAN: Will you say

a few words regarding prognosis in subclinical detachments? Is there any danger of subclinical detachment being made clinical by scleral indentation during examination?

DR. SCHEPENS replied that the prognosis of the subclinical detachment is generally very good; it is the only type of case in which we do a regular type of diathermy operation, as we used to do it years ago. I don't think that either my associates or I have observed a case where the retinal break was made bigger or where the detachment became more extensive by scleral pressure.

DR. CHAMLIN: How long have your oldest tubes been in? What is their ultimate fate?

DR. SCHEPENS said that the oldest tube has been in since January, 1952. Recently I saw one of the very early cases on which a circling tube had been used. This was over two years postoperatively. The functional result is good, and there is no visible buckle in the fundus. The latter is somewhat surprising and indicates that the 2-0 black silk which is passed through the lumen of the polyethylene tube has disintegrated thus permitting the intraocular pressure to push the tube slightly outward. As a result, the globe has regained its spherical shape. As far as we can tell, the polyethylene tubing is buried by newly formed connective tissue in the sclera. It causes very little reaction and probably remains there indefinitely.

DR. KRAVITZ: How often do you see late (that is, after one year or more) degeneration of the macula after successful retinopexy which originally did not involve the macular area.

DR. SCHEPENS said that such cases do occur and he has learned never to tell a patient how much he will see after the operation. What happens in some cases is that the hyaloid may shrink and cause traction upon the retina, in the region of the macula. This causes edema and later degeneration of the macula. As far as he knows, there is no way to prevent it.

DR. BERLINER: What has been your experience with late cures, that is, the retina

goes back two to three months after operation?

DR. SCHEPENS replied that such cases may result from three kinds of circumstances. In the first there is still a small break which is open in the retina, and the choroid cannot pump out the subretinal fluid fast enough for a rapid cure. In the second type of case the retina is held away from its normal position by fixed folds. Consequently, some detachment remains present for two or three months in spite of the choroid which pumps out subretinal fluid. Finally, a slow reattachment may be observed if the absorptive power of the choroid is damaged.

DR. KORNZWEIG: Have you seen any patients with tears of the retina that did not go on to form detachment and that persisted for as long as a year or more?

DR. SCHEPENS said he had. He considers that one of the puzzling problems in this field. In rare cases one observes large retinal tears which do not cause extensive detachment for a long time. In most cases, however, retinal tears lead to extensive retinal detachment after a period of time.

DR. THEODORE: Tell us a little more about the postoperative management with reference to no use of pinhole glasses.

DR. SCHEPENS said that they have been changing their postoperative management gradually. Today the typical management would be as follows:

The patient is placed in bed with a binocular dressing, the next day his good eye is uncovered, he gets out of bed, and sits up. The third or fourth day he is allowed to walk, and he is given his own glasses. If he shuns the light, he is given dark glasses. He is allowed to leave the hospital seven to eight days after the operation.

DR. POSNER: Why don't you use more perforating coagulations?

DR. SCHEPENS replied that he feels that the perforations are the most dangerous part of the operation. They may cause intraocular bleeding and vitreous loss. For this reason, we like to make one tiny hole in the

choroid and no more, provided we obtain a sufficient loss of subretinal fluid. We have seen many cases where a surgical failure followed the indiscriminate use of perforations. Examination of such cases reveals that aside from the original retinal breaks, there are sometimes as many as 15 man-made retinal holes caused by the diathermy points.

DR. FINLAY: What is your treatment of macular holes?

DR. SCHEPENS said that a break in the macula is extremely rare. Many of the published cases of successfully treated break in the macula undoubtedly showed no true macular break, because the relatively good postoperative vision reported is incompatible with such a lesion. In our experience only about one percent of all cases of retinal detachment show a break in the macula. Our treatment of this lesion consists in making one or two surface diathermy applications over the macular area, followed by one perforating diathermy application. Then a short polyethylene tube is sutured to the sclera, over the macular area. The indentation so produced lasts for three to four weeks. It is important that the tube should not press on the optic nerve as this may cause papilledema.

DR. CANTOR: Do you use your buckling operation in disinsertions?

DR. SCHEPENS said that he did; we feel that the percentage of success is higher and the recovery quicker with a buckling operation in this type of case.

DR. SAMUEL GARTNER: Do you operate on retinal detachments of two to three years' duration? Is there any time limit after which you would not operate?

DR. SCHEPENS replied that they do. As a rule, we feel that in any case of retinal detachment vision which has been lost for two years or more will not be recovered. Therefore, in a detachment which has been present for over two years we can hope for no more than the restoration and conservation of what vision was present two years previously. Bearing this in mind there is no

particular time limit. For instance, one patient was operated upon with benefit for a detachment which had been present for eight years.

DR. KRONENBERG: How do you feel about operating on a patient with retinitis proliferans?

DR. SCHEPENS said that he has done a certain number of those. I think that it is essential in such cases to determine whether or not the detachment is accompanied by breaks in the retina. If retinal breaks are found, and a scleral buckling operation is correctly performed, the patient generally derives benefit from the surgery.

DR. DOUGLAS: Are you now using a circling polyethylene tube in all your cases?

DR. SCHEPENS replied that he did not. We use one of the several procedures described by Dr. Okamura in this presentation. At present, however, a circling tube is used in over one half of the cases, and the trend is toward a wider use of this method. With the circling tube we have obtained a more pronounced buckling effect and, on the whole, we have so far had fewer complications than with a buried tube which was not circling the globe.

DR. ROULETTE: What effect did the polyethylene tube have on myopia in retinal detachment?

DR. SCHEPENS said that any type of scleral resection has an immediate effect upon the refraction. If the resection is not of even width all around the globe, it will cause astigmatism. Our experience with scleral buckling has been that the initial change in refraction is large at first but often lessens in the course of three to six months. This lessening, however, is not an absolute rule and permanent changes up to 20 diopters of spherical error and up to six diopters of cylindric error have been observed. In conclusion, this procedure is unreliable for the correction of either myopia or astigmatism.

Jesse M. Levitt,
Recording Secretary.

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Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Fifty reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Company, Inc., 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

MISUSE OF ACETAZOLAMIDE

Acetazolamide decreases the rate of aqueous secretion and thus lowers intraocular pressure in glaucomatous eyes in spite of the obstruction to aqueous outflow. This capacity of carbonic anhydrase inhibitors has led to their extensive clinical application. As with so many of the effective newer drugs in present-day medical therapeutics, initial

overenthusiasm resulted in misguided and excessive use. However, with the time and experience of over three and one-half years' use, the areas of usefulness as well as abuses of such agents are becoming defined more precisely.

The use of acetazolamide preoperatively in acute glaucomas or for short periods of time in transient or self-limited glaucomas

has proved a most valuable adjunct to standard forms of therapy. Furthermore, it has been established that selected patients with chronic glaucoma can be maintained normotensive for periods of over three years without further loss of visual field when acetazolamide is added to their therapeutic regimen.

In spite of impressive results with the above uses of carbonic anhydrase inhibitors, several instances of misuse can be delineated:

1. *Prolonged delay in surgical therapy of angle-closure glaucoma*

The availability of an agent that aids in reducing intraocular pressure in acute attacks of angle-closure glaucoma has led to an increased tendency to treat this condition medically. This has occurred in spite of ample evidence that in the presence of an adequate trabecular mechanism as determined by tonography, this type of glaucoma can be cured by the relatively simple and innocuous iridectomy. Not only has the long-term or prophylactic therapy of angle-closure glaucoma with carbonic anhydrase inhibitors proved almost uniformly unsuccessful but, by their use, the opportunity is often missed for effecting a surgical cure. By attempting such medical therapy, the curable stages of this disease process are often permitted to go on into the stages of extensive anterior synechias and ocular damage. Iridectomy is no longer curative and filtering procedures become necessary in spite of their inherent complications and inadequacies.

2. *Inadequate dosage*

When chronic simple glaucoma becomes uncontrolled on miotics most patients will require 250 to 500 mg. of acetazolamide every four to six hours for adequate therapeutic response. The use of occasional small doses of Diamox is indicated in some advanced secondary glaucomas, but rarely improves the status of control in most patients. The assumption that a single measurement of intraocular pressure in the ophthalmologist's office is representative of the around-

the-clock level is a common source of error in establishing the dose and frequency of administration needed by a given patient.

3. *Unnecessary use*

The addition of acetazolamide to the therapy of a patient with chronic simple glaucoma adequately controlled on miotics is entirely unnecessary. Nevertheless, for various reasons, there appears to be an increasing tendency to treat more and more glaucomatous patients with acetazolamide. In some instances (for example, lens opacities) acetazolamide has been used to replace miotic therapy. There would appear to be little rationale for such substitution therapy with an agent which has extensive systemic effects. Routine postoperative use, especially after filtering operations, the long-term therapy of unilateral absolute glaucoma, and the prolonged administration in traumatic hyphemas are also becoming recognized as contraindications to systemic carbonic anhydrase inhibition.

4. *Failure to appreciate systemic toxicity*

One of the principal objectives of current clinical research on acetazolamide and related compounds is the resolution of the problem of disabling systemic side effects. Thus, over one-third of all patients begun on long-term Diamox therapy have had to stop because of intolerable side effects, such as anorexia, excessive fatigue, or ureteral colic. As difficult as it may prove in a busy office, the ophthalmologist who chooses to use these agents must be constantly on the alert for the appearance of these or other unrecognized toxicity or side effects. For example, the awareness that ureteral colic could occur as a consequence of acetazolamide administration in some patients led to the discovery of a sizable unrecognized group of patients with this complication. It is of incidental interest that the occurrence of this complication has resulted in the interesting finding that acetazolamide administration uniformly leads to a dramatic fall in the urinary citrate excretion in man. Such a decrease in urinary citrate has previously

been reported to occur along with renal calcification in the rat treated with Diamox. The role of citrate in chelating and solubilizing calcium in the urine of patients as well as the relationship to ureteral colic of its altered concentration after acetazolamide administration remain speculative.

With increasing knowledge of the nature and mechanisms of aqueous secretion, one may anticipate more effective and less toxic medical means of altering aqueous flow. Already, newer carbonic anhydrase inhibitors are available which can lower intraocular pressure with much less renal or gastrointestinal effects. There are excellent prospects for compounds with even greater ocular specificity. It should be remembered, however, the basic defect in glaucoma is almost always an obstruction to aqueous outflow. If this obstruction can be relieved medically (for example, by miotics in chronic simple glaucoma) or surgically (for example, by iridectomy in uncomplicated angle-closure glaucoma), such measures which can correct the defect are much to be preferred to the palliation afforded by secretory suppression. The carbonic anhydrase inhibitors should be reserved as useful adjuncts to be added to these measures when necessary for the lowering of intraocular pressure.

Bernard Becker.

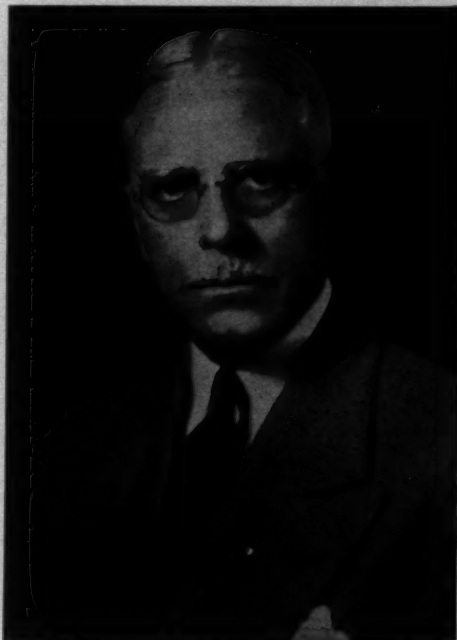
OBITUARY

THOMAS D. HEED
(1875-1957)

In the death of Mr. Thomas D. Heed, on January 29, 1957, at his home at 565 Picacho Lane, Santa Barbara, California, ophthalmology lost a great benefactor.

Mr. Heed was a man of imagination and foresight. He, jointly with his wife, Ruth Byers Heed, established the Heed Ophthalmic Foundation, whose primary object has been to further the studies and educational opportunities of outstanding young Ameri-

can ophthalmologists, and it is in this connection that he will be known in ophthalmic circles for generations to come. The foundation is a unique organization, conceived by Mr. Heed in conjunction with his wife, who survives him and who is dedicated to carrying



THOMAS D. HEED

on the activities and interests of the foundation. It was established in 1945, at which time a small board of men outstanding in the profession was created by them, and the First National Bank of Chicago was appointed trustee of the funds.

It was Mr. Heed's joy to see some of the results of the fellowships which he made possible during his life time, rather than to provide for such a foundation after the death of himself and his wife. He, therefore, allocated certain sums of money throughout the intervening years, as a result of which 41 young men have been enabled to progress further with their careers and their studies and thus make greater contributions to oph-

thalmology than would otherwise have been possible. To the great good fortune of ophthalmology, Mrs. Heed is planning to continue this wonderful and unusual foundation, as carried on by Mr. Heed during his lifetime and, at the time of her death, according to his wishes, funds will be laid aside in order that it may be continued in perpetuity.

Mr. Heed was well known for his activities, other than those related to young students of ophthalmology. He was active and successful in the business world, both of Chicago and New York. He was born in Saint Louis, in 1875. From there he went to college in Emporia, Kansas, and entered the railroad service in the general auditor's office of the M. K. and T. Railroad. He then became cashier of the Southwestern Passenger Bureau and chief clerk of the treasury department of the St. Louis and San Francisco Railroad. He later became assistant secretary and treasurer of the same road, and still later held the same offices in the Chicago and Eastern Illinois Railroad. In 1913-15 he was president of the latter, and later became its receiver. From 1921 to 1931 he was a director of this road, and also of the St. Louis and San Francisco Railroad. He was president and director of many outstanding companies, with varying interests; especially was he associated with land and mining interests in the West. Still other interests were in the lumber business. One of the last of these was that of director of the Edward Hines Lumber Company, of Chicago.

From 1942 to 1945, he served as chairman of the Chicago Division of the United States Navy Price Adjustment Board, in connection with which, in January, 1946, he received the Navy's highest civilian award for outstanding service with this board from October, 1943, to January, 1946.

Mr. Heed was well known socially, both in Chicago and New York. He was a member of the Midway and Tavern Clubs of Chicago, and the Midway Club of New York.

Mr. Heed's was a delightful, kindly but firm personality. On meeting him, he put one at ease, and made one feel his deep interest in the human beings about him. The direction of the interests of Mr. and Mrs. Heed toward ophthalmology was initiated by difficulties which both had experienced with ocular disturbances in their early years, and it was out of gratitude for the fortunate outcome of these difficulties that the Heed Ophthalmic Foundation was established.

M. Hayward Post.

CORRESPONDENCE

RETINOPATHY OF IMMATURITY

Editor,

American Journal of Ophthalmology:

In the paper on "Retinopathy of immaturity" by Habegger, et al. (*Am. J. Ophth.*, 42:377 [Sept.] 1956), it is stated that the early manifestations of retrolental fibroplasia are dilatation and tortuosity of retinal vessels and frequent retinal hemorrhages.

This I believe to be incorrect. The earliest manifestation is marked contraction of the retinal vessels. When early and regular examination of the infant has been possible, this stage precedes the stage of very marked dilatation.

The effect of high oxygen therapy in constricting the retinal vessels has led to the belief in its curative and prophylactic value with the unfortunate result of increasing the number of blind infants.

I would also suggest that the finding of retinal hemorrhages soon after birth in a premature infant would have no more significance than the more common finding of retinal hemorrhages in the newborn, full-time child.

I have only once seen a retinal hemorrhage in a day-old premature infant, but most of these infants are too feeble to permit adequate examination.

Any suggestion that hypoxia is the cause of retrolental fibroplasia is to be deprecated.

A careful study of the literature has not revealed an authentic case of retrolental fibroplasia which has not been subjected to oxygen therapy.

(Signed) J. Berkson,
Liverpool, England.

DR. INGALLS' REPLY

Editor,
American Journal of Ophthalmology:

Dr. Berkson says that it is incorrect to state that the early manifestations of retrolental fibroplasia are dilatation and tortuosity of retinal vessels. Is he not confusing the disease with the disturbance that precedes it? I wonder if he would be willing to make a diagnosis of retrolental fibroplasia merely because he observed "marked contraction of the retinal vessels." I doubt it. In any event we were referring to early manifestations, not necessarily the earliest.

Dr. Berkson further states that the "effect of high oxygen therapy in constricting the retinal vessels has led to the belief in its curative and prophylactic value." I think he has the historic sequence of events backward. Oxygen therapy came first, whereupon the disease made its appearance; and for a decade all investigators were working in the dark. Since 1954 there has been no difficulty in controlling the disease and there is not much need for a voice crying in the wilderness in 1957.

Most would agree with Dr. Berkson's statement about retinal hemorrhages soon after birth. I do not see that his own statement of having seen retinal hemorrhages once in a day-old premature infant needs comment.

His final pronouncement that "any suggestion that hypoxia is the cause of retrolental fibroplasia is to be deprecated" side-steps the question of pathogenesis. Why do the physiologists find systemic hypoxia as a sequel of hyperoxia? Why the pulmonary lesions in experimental animals? Why have physiologists coined the descriptive phrase, hyperoxic hypoxia? If 40-percent oxygen is

to be regarded as the permissible ceiling—which it is by general consent—does this mean that it is malpractice to give 42-percent oxygen for a few minutes? What about a few hours? What is the gaseous component of commercial oxygen which oxydizes potassium iodide? Is it a microquantity of ozone? (Dr. John R. Suydam of Boston has been working on this problem in the laboratory of the Department of Epidemiology.)

My own opinion is that the last word has not been said on the irritant properties of oxygen (or contained gases), their relation to pulmonary hyaline membrane, systemic anoxia, and retrolental fibroplasia. Hence experimental work goes on of the sort that has given rise to Dr. Berkson's comment.

(Signed) Theodore H. Ingalls,
Boston, Massachusetts.

BOOK REVIEWS

CHILDREN'S EYE PROBLEMS. By Emanuel Krinsky, M.D. New York, Grune and Stratton, Inc., 1956. 166 pages, 33 figures, references, index. Price: \$6.00.

The author, whose book *The Management of Binocular Imbalance*, published in 1948, attracted much favorable attention, has placed in our hands this time a short but surprisingly complete volume that deserves popularity. It is especially designed for pediatricians and nurses working with the eye problems of children and, as such, is written in a somewhat simplified form.

There are six chapters, which cover the eye and its development, normal ocular phenomena, the examination, eye symptoms and signs, eye disorders mainly of local origin, other eye diseases, systemic diseases, and problems in management, which is particularly good. The discussions on glaucoma, cataract, and cross-eye or strabismus are particularly noteworthy.

It should be a particularly useful book to send or give to a pediatrician or general practitioner, provided he doesn't purchase it himself. It is, however, doubtful that the

fully trained ophthalmologist will appreciate it very much, for actually it was not written for him. It is excellent for its purpose.

Derrick Vail.

PHYSIOLOGY OF THE OCULAR AND CEREBROSPINAL FLUIDS. By Hugh Davson, D.Sc. Boston, Little, Brown and Company, 1956. 388 pages, 109 figures, bibliography, index. Price: \$14.00.

One of our leading neurologists has long contended that ophthalmologists are basically neurologists who have made a specialty of cranial nerves II to VII and their central connections. That there is much truth in this statement is evidenced by the fact that ophthalmologists have always been intrigued by the similarities between the cerebrospinal fluid and the aqueous humor. With the ever-increasing complexity of the physiology of the latter, however, it becomes more and more difficult for the student of ophthalmology to learn all the details of his own fluid, much less his neighbor's. Dr. Davson, however, is that rare student, and in this detailed and comprehensive textbook he demonstrates the current pedagogic maxim that much can be learned by abolishing traditional departmental lines and allowing fertile minds in different fields to cross-pollinate each other. This book is indeed a sturdy hybrid.

The first section is devoted to the anatomic characteristics of the tissues producing the bathing fluids of the eye and central nervous system, and these two chapters are unusually detailed for a textbook of physiology. There follows a discussion of the composition of the fluids, the mechanisms of production, the nature of the blood-fluid barrier, and a final section on fluid pressures.

The formation of aqueous humor has long been a special love of Dr. Davson's, and this book is essentially a marshalling of the evidence for his theory of formation of both aqueous and cerebrospinal fluid. He feels that, in the case of the eye, aqueous is formed first by a special secretory activity of

the cells of the ciliary epithelium and secondly by a diffusion of water and salts from the blood vessels of the iris. This is quite at variance with the mechanism proposed by Friedenwald and elaborated by Kinsey, although the terms secretion and diffusion appear in both. He gives short shrift to the hypotheses developed by these workers. His objections are many, but they center about the fact that in many cases the data for certain substances are not true for all species, that many of the experiments were unphysiologic in regard to the stresses applied, and that the theories are too conjectural for the little data available. For example, although Davson agrees that Diamox is a potent agent in decreasing aqueous formation by inhibiting the formation of carbonic acid, he feels that the latter may be only one step in the chain of events leading to the formation of the complex substance called aqueous humor rather than the basic mechanism postulated by Friedenwald.

It would be unfair not to point out that the late Jonas Friedenwald was well aware that a hypothesis was only a hypothesis and that he always felt that *at the moment* the particular theory advanced by him gave the best fit for the data available. Some of the data presented by Dr. Davson are equally controversial, and this is all to the good, since in scientific investigation, unlike political investigations, the term "controversial" is stimulating and admirable rather than pejorative.

The bibliography at the end of each chapter is extensive and brings together in one volume a rather complete survey of the literature.

David Shoch.

SAMUEL GRIDLEY HOWE, SOCIAL REFORMER.

By Harold Schwartz. Cambridge, Harvard University Press, 1956. 348 pages, bibliography, index. Price: \$6.00.

On graduating from Harvard Medical School in 1824, Samuel Gridley Howe, M.D., followed Byron's example and for the

next six years was in the service of embattled Greece. One of his exploits, the rescue of a wounded soldier, is commemorated in Whittier's *The Hero*. Howe toiled in the battlefield, organized hospitals, directed American relief, founded an agricultural colony, and administered public-work projects. Eventually his interest in relieving the ills of man shifted from the physical to the social and, on his return, he gladly accepted an appointment as director of the projected New England Asylum for the Blind. By 1843 the Perkins Institution, as it was then known, had become world famous and fostered the creation of similar schools in other states. Howe had conceived the possibility of educating the deaf-blind, a project never before successful. Laura Bridgman and Oliver Caswell were the first such students. Dickens in *American Notes* gave a rapturous account of their achievements, which thus attained world-wide attention. Howe also proved, in an experimental class at Perkins, that the feeble-minded could benefit from schooling and as a consequence the now famous Walter E. Fernald School was established.

The many-sided Howe became a director of the Massachusetts General Hospital, aided Horace Mann in educational reform, and seconded Dorothea Dix in obtaining proper care for the insane. After the annexation of Texas, Howe devoted himself to antislavery agitation and was a financial backer of John Brown. During the Civil War he was assigned to the inspection of troops and emphasized repeatedly the need of greater cleanliness and hygiene. On one of his trips, in the fall of 1861, his wife, Julia Ward Howe, wrote the inspired *Battle Hymn of the Republic* which, next to Lincoln's addresses, best expressed the spirituality of the Northern cause.

This fascinating biography of a great

American is Volume 67 of the Harvard Historical Studies and is a notable literary as well as historical contribution.

James E. Lebensohn.

NEUROLOGY OF THE OCULAR MUSCLES. By David G. Cogan, M.D. Springfield, Illinois, Charles C Thomas, 1956, edition 2. 284 pages, 86 illustrations, 2 color plates, 1,141 references, index. Price: \$8.50.

The well-known author is professor of ophthalmology, Harvard Medical School, and director of the Howe Laboratory of Ophthalmology, Boston, Massachusetts. He has elaborately revised the first edition of his useful book that appeared in 1948, and has rewritten some chapters, rearranged and expanded others. In many respects it is, therefore, a completely new book on a difficult subject in which he is thoroughly at home.

The knowledge of this subject has increased a lot since 1948, thanks mostly to the new tools for investigation that have subsequently appeared. Dr. Cogan has played a conspicuous part in adding original discoveries to our information, for example, ocular dysmetria, a work for which he received the Knapp Medal of the Section of Ophthalmology, A.M.A., in 1955.

Those who have read and carefully studied the first edition will recall the author's fluent prose with pleasure, and the meticulous care with which he correlated the objective signs and symptoms of a given ophthalmoneurologic problem pertaining to the ocular muscles with a clear description of the neuro-anatomy and pathology involved. This fluency and careful documentation will be found liberally expanded in the second edition.

The book is beautifully printed and clearly illustrated.

Derrick Vail.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

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| 1. Anatomy, embryology, and comparative ophthalmology | 10. Crystalline lens |
| 2. General pathology, bacteriology, immunology | 11. Retina and vitreous |
| 3. Vegetative physiology, biochemistry, pharmacology, toxicology | 12. Optic nerve and chiasm |
| 4. Physiologic optics, refraction, color vision | 13. Neuro-ophthalmology |
| 5. Diagnosis and therapy | 14. Eyeball, orbit, sinuses |
| 6. Ocular motility | 15. Eyelids, lacrimal apparatus |
| 7. Conjunctiva, cornea, sclera | 16. Tumors |
| 8. Uvea, sympathetic disease, aqueous | 17. Injuries |
| 9. Glaucoma and ocular tension | 18. Systemic disease and parasites |
| | 19. Congenital deformities, heredity |
| | 20. Hygiene, sociology, education, and history |

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Coulombre, Alfred Joseph. **The role of intraocular pressure in the development of the chick eye.** A. M. A. Arch. Ophth. 57:250-253, Feb., 1957.

The normal expansion of the cornea during development is dependent, among other factors, on the tangential forces generated in the wall of the eye by an expanding vitreous body. (1 figure, 11 references)
G. S. Tyner.

François, J., Neetens, A. and Collette, J. M. **Vascularization of the optic pathways. No. 5. Chiasma.** Brit. J. Ophth. 40: 730-741, Dec., 1956.

Twenty-two human specimens are used to investigate the vascularization of the chiasm. The techniques used include dissection after fixation in 10-percent formaldehyde, injection of India ink, staining with benzedrine, and microradiography. The internal carotid, anterior cerebral and the anterior communicating arteries are the chief sources of supply. In one-third of the cases a collateral vessel from the anterior communicating artery was found. The chiasma is to a slight extent invaded

by a fine network of vessels from the optic nerve and optic tract. Seven separate and distinct capillary zones could be identified at the chiasm. (15 figures, 6 references)
Lawrence L. Garner.

Liss, Leopold. **The astroglia of the human optic nerve, chiasm and tract: a study with silver-carbonate.** J. Comp. Neurol. 105:151-160, Aug., 1956.

Details are given of variations in the silver-carbonate technique used. Examination of stained human material revealed four types of astrocytes in the central and lateral portions of the optic nerve. These are described as fibrillar, giant, V-shaped, and small. The pattern of the astroglia appeared to be adjusted to the course of the nerve fibers. Details of the morphology in other portions of the chiasm and tract also are given. (1 figure, 2 plates, 6 references)
Harry Horwich.

Liss, L. and Wolter, J. R. **The nerve supply of the bloodvessels in the human optic nerve.** Klin. Monatsbl. f. Augenh. 129:793-799, 1956.

An optic nerve was examined after the globe had been enucleated 16 years earlier. All centripetal fibers had disappeared and only the centrifugal and perivascular

nerves remained. Two types of fibers were found with silver carbonate staining. It is assumed that this speaks for an autonomic double innervation of these blood vessels. (8 figures, 12 references)

Frederick C. Blodi.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Bietti, G. B. **Unsolved problems and recent advancements in ocular virology.** Boll. d'ocul. 35:161-190, March, 1956.

The author presents an excellent review of the present status of ocular virology. An extensive bibliography is included.

William C. Caccamise.

Büttner-Wobst, W. and Mietke, H. **Histologic observations on three eyes after local streptomycin treatment.** Klin. Monatsbl. f. Augenh. 129:731-737, 1956.

Two eyes had a severe infection following a perforating injury and one eye a late infection after a trephine operation. They all showed a marked perivasculitis in the conjunctiva, episclera and uvea. This chronic inflammation is perhaps caused by a tissue necrosis which occurred during the acute phase. The latter was suppressed by the frequent subconjunctival injection of streptomycin which by itself does not damage the eye. (3 figures, 30 references)

Frederick C. Blodi.

Christensen, L., Beeman, H. and Allen, A. **Cytomegalic inclusion disease.** A. M. A. Arch. Ophth. 57:90-99, Jan., 1957.

Cytomegalic inclusion disease is a multisystem mostly in the newborn which is characterized pathologically by an inclusion-containing giant cell that appears predominantly in epithelial linings of visceral and cerebral epithelium. From the viewpoint of the ophthalmologist the clinical findings simulate toxoplasmosis and possibly measles in the first trimester. These include retinopathy, intracranial

calcification and cataract. A case is reported. 10 figures, 10 references)

G. S. Tyner.

Janes, R. G. and Ellis, P. P. **Vascular changes in eyes of diabetic rats.** A. M. A. Arch. Ophth. 57:218-223, Feb., 1957.

The authors have observed anterior segment hemorrhages and corneal vascularization in rats with severe chronic diabetes. (8 figures, 8 references)

G. S. Tyner.

Millwood, E. G. and Klein, M. **Behavior of Ps. pyocyanea in different concentrations of penicillin.** Brit. J. Ophth. 40:656-660, Nov., 1956.

The object of this work was to determine whether penicillin solutions can be protected against contamination with Ps. pyocyanea by incorporation of a preservative which would not affect the potency of the penicillin. Several such preservatives were used in controlled experiments in various strengths of penicillin. It was discovered that growth varied considerably with the strength of the solution since Ps. pyocyanea grows very well in weak solutions of penicillin and remains viable in the solution for a long time. In strong solutions of the drug, the bacteria did not survive at all. Thiomersalate in 0.002 percent concentration served very well and also was compatible with penicillin. (2 figures, 2 tables, 6 references)

Morris Kaplan.

O'Connor, G. **Anti-Toxoplasma precipitins in aqueous humor.** A. M. A. Arch. Ophth. 57:52-57, Jan., 1957.

The author found a precipitating antibody to Toxoplasma gondii in the aqueous of four patients with presumptive toxoplasmic uveitis. This antibody and a precipitin obtained in purified gamma-globulin fractions of serum from patients with high Toxoplasma dye test titers seem to be identical. (5 figures, 5 references)

G. S. Tyner.

Weil, V., Laval, J. and Sturman, R. **Escherichia coli panophthalmitis from pyelonephritis.** A. M. A. Arch. Ophth. 57: 58-64, Jan., 1957.

The literature of endogenous infection of the eye is briefly reviewed. This case is unique in that the causative organism was found by culture in the urine, the blood, and the eye. (32 references)

G. S. Tyner.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alekseeva, V. **The influence of insulin on the permeability of the lens capsule.** Vestnik oftal. 5:61-64, Sept.-Oct., 1956.

The influence of insulin on the permeability of the anterior and posterior capsules of the lenses of cattle was studied. The technique of preparing the capsules, the solution used and the measurement of the ascorbic acid are described in detail. To the solutions containing the capsule, 0.5 cc. of insulin was added. Two series of experiments were made. In the first five experiments the permeability of the anterior capsule to ascorbic acid was studied and in a second five that of the posterior capsule. In the second part of the experiment, 10 anterior and 10 posterior capsules were studied for the influence of insulin on the permeability of the capsule for ascorbic acid. In all experiments the second eye of the animal served as control.

This study showed that insulin decreases the permeability of both the anterior and posterior capsules for ascorbic acid. The permeability of the posterior capsule is decreased to a greater extent than that of the anterior capsule, namely: the average decrease of permeability of the anterior capsule is 17 or 78 percent, while for the posterior capsule it is 45 or 98 percent. The marked influence of insulin on the permeability of the posterior capsule may to a certain degree explain

the opacities of the lens in the posterior layers in diabetic cataract.

Olga Sitchevska.

Alfonso, G. F. **The action of a synthetic substance having the chemical effect of the corticosteroids.** Boll. d'ocul. 35:122-129, Feb., 1956.

The author discusses a synthetic preparation with cortisone effects. The clinical results obtained in the treatment of patients with iritis, iridocyclitis, uveitis, and keratitis, were favorable. (8 references)

William C. Caccamise.

Allen, J., Manning, J., Guidry, M. and Kelly, J. **Changes in aqueous flow and blood-aqueous barriers after hydrochloric acid burns to the eye.** A. M. A. Arch. Ophth. 57:1-6, Jan., 1957.

Previous work in this laboratory showed that the ascorbic and lactate concentrations in the anterior aqueous humor of rabbits decrease after the onset of hydrochloric acid injury to the cornea. In the present experiments the results show that there is an increase in the rate of flow of aqueous humor as well as an increase in permeability of the blood-aqueous barrier in these acid-injured eyes. (2 figures, 3 tables, 5 references)

G. S. Tyner.

Ambrosio, A. **The behavior of carbonic-anhydrase activity of the cornea and of the retina in the course of an inflammatory process of the uvea.** Boll. d'ocul. 35:445-450, June, 1956.

The author found no appreciable changes in the carbonic-anhydrase activity of the retina in the course of an inflammatory process which was experimentally produced in the uvea of rabbits. (1 table, 25 references)

William C. Caccamise.

Auricchio, G. **Studies in cataracta complicata: the ascorbic acid-dehydroascorbic**

acid equilibrium in the ocular tissues and fluids in normal conditions and in the course of an inflammatory process of the uveal tract. *Boll. d'ocul.* 35:217-228, March, 1956.

Animal studies revealed that intraocularly there normally exists a gradient of concentration of dehydroascorbic acid with a maximum in the anterior uvea and a minimum in the lens. The reverse applies to the level of ascorbic acid. A decrease in the concentration of ascorbic acid in the intraocular fluids and tissues occurs in the course of an inflammatory process of the uveal tract. The reversible oxidized form of ascorbic acid shows a simultaneous relative increase, so that the ratio of the reduced to the reversibly oxidized form demonstrates a distinct decrease from the normal value. This phenomenon is particularly evident in the lens where normally there is only a trace of the oxidized form. In addition, there is a disappearance of the normal protective mechanism that the lens has against the auto-oxidation of ascorbic acid. (2 tables, 33 references)

William C. Caccamise.

Boles-Carenini, B. **The effects of a sympathicomimetic substance—isonephrine (Neosynephrine)—on the ocular tension and on the dynamics of the aqueous humor.** *Boll. d'ocul.* 35:412-422, June, 1956.

The author briefly summarizes the chemical and pharmacologic properties of Neosynephrine and its principal indications in ophthalmology. Electronic tonography was carried out on normal and glaucomatous eyes before and after the instillation of two drops of 10-percent Neosynephrine. The ocular tension, the facility of outflow, and the production of aqueous of the normal eyes were not significantly influenced by the application of the Neosynephrine. In the eyes that had chronic simple glaucoma and secondary

glaucoma, the Neosynephrine caused a decrease in the ocular tension. The facility of outflow was increased in these cases, although there was no change in the production of aqueous. In eyes with congestive glaucoma, the Neosynephrine did not cause a decrease in the ocular tension. On the contrary, there was at times an increase in the tension due to a decrease in the facility of outflow of the aqueous. Therefore, while the application of Neosynephrine is advisable in chronic simple glaucoma and secondary glaucoma, it is probably contraindicated in congestive glaucoma. (6 tables, 15 references)

William C. Caccamise.

Breinin, Goodwin M. **Electromyographic evidence for ocular muscle proprioception in man.** *A. M. A. Arch. Ophth.* 57:176-180, Feb., 1957.

The author believes that proprioception exists in the extraocular muscles but it is not implied that it provides awareness of position. (6 figures, 6 references)

G. S. Tyner.

Caballero del Castillo, Daniel. **The permeability of the blood-aqueous barrier.** *Arch. Soc. oftal. hispano-am.* 16:663-665, July, 1956.

By biologic experiments on rabbits the author confirmed Sulman's finding that the melanophore hormone and ACTH are identical substances. Ray K. Daily.

DalSanto, G., Delogu, A. and Campus, S. **The pathogenesis of cataracta complicata.** *Boll. d'ocul.* 35:423-435, June, 1956.

A study was made of the passage of P32 into the aqueous humor of rabbits. The penetration of this substance into the lens during the course of an inflammatory process (experimentally induced anaphylactic uveitis) was also studied. The authors were also attempting to answer the question whether an altered up-take of P32 would throw some light on the

lens changes that occur in the course of uveitis. (3 tables, 22 references)

William C. Caccamise.

De Conciliis, U. **Insulinase in the ocular fluids and tissues.** *Boll. d'ocul.* 35:112-121, Feb., 1956.

The author studied the insulinase in normal and pathologic ocular fluids and tissues in cattle and rabbits. He found that the insulin inhibition that is found in ocular fluids that contain blood and exudates can be attributed to the presence of constituents of blood. The inhibition that is found in a cataractous lens is the result of the proteolytic activity in such a lens. (2 tables, 36 references)

William C. Caccamise.

Falcinelli, G. **Experimental investigation of the passage of achromycin into the anterior chamber.** *Boll. d'ocul.* 35:302-313, April, 1956.

The author's experiments with rabbits indicated that the intravenous administration of achromycin resulted in a rapid appearance of the drug in the anterior chamber. Similar results were obtained when the drug was injected subconjunctivally. Although the intramuscular administration of achromycin resulted in anterior chamber levels that were lower than those produced by both intravenous and subconjunctival administration, the author considered the aqueous level to be therapeutically adequate. An effective aqueous level of achromycin resulted from oral administration only after multiple dosages. (6 figures, 9 references)

William C. Caccamise.

François, J., Rabaey, M., Wieme, R. and Evens, L. **Electrophoretic study of the influence of pH on lens proteins.** *Ann. d'ocul.* 189:611-618, July, 1956.

The electrophoretic pattern for soluble lens proteins remained the same after dialysis of the protein solution against buffer solutions of different pH between

4 and 8.6. Acidification of the solution to a pH lower than 3.5 produced a denaturation and flocculation of fractions I and II. The third fraction was more resistant and remained visible on the pattern. Alkalization to a pH above 9 did not produce flocculation, but there was no longer a clear separation between fractions I and II but the third fraction was more resistant here also and remained visible even after 24 hours of alkalization at pH 10.5. (4 figures, 2 tables, 9 references)

John C. Locke.

François, J. and Rabaey, M. **The existence of an embryonic crystallin.** *Bull. Soc. belge d'opht.* 113:359-372, June, 1956.

About 30 bovine lenses were studied to establish the origin of fraction III (gamma-globulin). The smallest lens examined was from an embryo 3.5 cm. long, the oldest from a 10-year-old ox. Paper electrophoresis, colorimetric biuret method or microkjeldahl were used. In the embryonic lens fraction III was found in high concentration, about 18 to 24 percent of the total protein. During this period fraction III increases equally in amount with fractions I and II. After birth fractions I and II continue to increase while fraction III diminishes. Only small amounts of the latter fraction are detected in the lens nucleus and just traces in the cortex of the mature lens. Fraction III nevertheless represents a distinct entity among the proteins, and is constituted only in embryonic life in the ox. It does not represent a product of denaturation of the aging alpha-crystallin. Its detection and classification was only accomplished with the help of paper electrophoresis. (17 figures, 4 tables, 14 references)

Alice R. Deutsch.

Fraser, H. **Oxyphenonium bromide as a mydriatic.** *Brit. J. Ophth.* 40:751-753, Dec., 1956.

Oxyphenonium bromide (Antrenyl) is

an autonomic ganglion-blocking agent and has an anticholinergic action similar to that of atropine. In this study a 5-percent solution was used in a 1:5,000 benzalconium chloride base. In 75 patients who had been found sensitive to all cycloplegics, this solution was used with excellent results. In only two cases was it necessary to discontinue the use of this preparation. Pupillary dilatation occurs within 37 to 80 minutes and persists for 10 to 21 days after the instillation of only one drop. Mydriasis seems to be at least as good as that of atropine. (1 table, 4 references) Lawrence L. Garner.

Green, H., Mann, M. and Waters, L. **Elaboration of bicarbonate ion in intraocular fluids. 1. Aqueous humors, following intravenous infusion of sodium bicarbonate.** A. M. A. Arch. Ophth. 57:76-84, Jan., 1957.

In order to get a better understanding of the mechanism of the formation of the bicarbonate ion in intraocular fluids, the authors studied the relationship between the bicarbonate ion concentration in the blood plasma and that in the aqueous humor. They conclude that the source of the bicarbonate ion in the aqueous is not completely explained by current concepts and theories. (3 tables, 10 references)

G. S. Tyner.

Green, H., Sawyer, J. and Leopold, I. **Elaboration of bicarbonate ion in intraocular fluids. 2. Vitreous humor, normal values.** A. M. A. Arch. Ophth. 57:85-89, Jan., 1957.

The authors attempted to determine the distribution of the ion in the vitreous humor and to correlate this with the concentration in the blood plasma and aqueous humors of the anterior and posterior chambers. They believe from their experiments that no definite conclusions can be drawn concerning the route of entry of bicarbonate ion into the vitreous humor

from a knowledge only of the distribution of the ion in that fluid. (9 references)

G. S. Tyner.

Guzzinati, G. C. and Salvi, G. **Alcian 8 G N and the mucopolysaccharides of the cornea.** Boll. d'ocul. 35:321-329, May, 1956.

The presence and the significance of the mucopolysaccharides in the ocular tissues and particularly in the cornea have been the object of numerous investigations. The authors report the results of their studies on the staining of corneal tissue by Alcian 8 G N. This stain proved itself to be orthochromatic and to have an affinity for acid mucopolysaccharides. (1 figure, 39 references)

William C. Caccamise.

Hagihara, T. **Pupillary movement of removed eye. I-III.** Acta Soc. Ophth. Japan 60:1869-1880, Dec., 1956 and 61:104-107, Jan., 1957.

In the enucleated eye of such animals as frog, toad, rabbit and dog, a pupillary contraction results upon exposure to an intensive illumination. The reaction occurs even in the iris taken out of the eyeball. The pupil of the removed eye of dogs and rabbits reacts also to a high temperature (60°C). The light reaction of the removed eye can occur for about two to four hours after the removal of the eye when kept in a balanced salt solution. The miosis produced by a high temperature can occur for 14 hours after the removal. A miosis by eserine can take place for an additional two hours after the cessation of the temperature reaction. (5 tables, 21 references)

Yukihiko Mitsui.

Heald, K. and Langham, M. E. **Permeability of the cornea and the blood-aqueous barrier to oxygen.** Brit. J. Ophth. 40:705-720, Dec., 1956.

A series of tests is described, in which live rabbits were used to ascertain whether or not the respiratory require-

ments of the corneal tissues could be obtained by the diffusion of oxygen from the aqueous humor. Contrary to previous reports, oxygen was found to move freely in either direction across the cornea, nor was this property significantly affected by removal of epithelial or endothelial layers. Although capable of diffusing from the aqueous to the cornea, the amount calculated is insufficient for the epithelial requirements, and the balance of oxygen is therefore obtained from the atmospheric oxygen anterior to the cornea as well as the oxygen obtained from the contiguous tissues. Altering the blood flow through the ciliary processes had no significant effect. (5 figures, 5 tables, 25 references)

Lawrence L. Garner.

Heinrichs, D. J. and Harris, J. E. **Lens metabolism as studied with the reversible cation shift.** *A. M. A. Arch. Ophth.* 57: 207-213, Feb., 1957.

The extent to which a return to normal cation concentrations occurred in rabbit lenses during incubation at 37°C after a cold-induced cation shift, was observed to bear an inverse relationship to the age of the lens. The different responses of young as compared with older lenses may be due to the utilization of different metabolic pathways by young lenses. (7 figures, 21 references)

G. S. Tyner.

Ibaraki, Y. **Influence of kallikrein (Bayer) on the retinal blood vessels and its relation to the autonomic nervous system.** *Acta Soc. Ophth. Japan* 60:1500-1520, Oct., 1956.

When kallikrein is injected into normal individuals, 10 units intramuscularly, a dilatation of retinal blood vessels takes place, usually in both artery and vein and rarely in one of them alone. When the same agent is injected into sympatheticotonic patients with essential hypertension and Bürger's disease, the retinal artery

reacts more intensively than the vein. The converse occurs in vagotonic patients with hypotension. Ibaraki concludes, therefore, that an observation of retinal vessels after an injection of kallikrein may give an indication of the balance of the autonomic nervous system of the patient.

When the agent is injected subconjunctivally, a dilatation of retinal vessels also follows. This fact may indicate that the agent has a local action. (12 figures, 16 tables, 26 references) Yukihiko Mitsui.

Inoue, W. **A study of lens protein. I-III.** *Acta Soc. Ophth. Japan* 60:1612-1617, 1633-1636, 1695-1698, Oct., Nov., 1956.

The paper electrophoresis picture of the lens protein of various animals is first described. Then Inoue states that with the development of naphthaline cataract, a rapid decrease of water-soluble protein occurs, particularly of the alpha-crystalline of the lens cortex and nucleus. The protein of the embryonic lens is also discussed. Alpha-crystalline appears only in the later half of the embryonic life in the chick. (17 figures, 25 references)

Yukihiko Mitsui.

Kamouchi, T. **Electromyographic studies of ocular muscles. Time series analysis of current discharge interval of neuromuscular unit spikes.** *Acta Soc. Ophth. Japan* 60:1675-1686, Oct., 1956.

This is a time series analysis on the electromyogram of discharge interval of neuromuscular unit spikes. Two types of the waves are distinguished; one is a slow undulation and the other is an irregular fluctuation. The slow undulation wave seems to be complicated in nature. There is no agreement between the cycle of this wave and any cyclic phenomenon of a living body. The irregular fluctuation is further divided into two subtypes; harmonic and nonharmonic. In the harmonic waves, only the C-wave of Nomura is recognizable and not the S-wave (Nomura

S. Recent advance in electromyography, Nagai & Co., Kyoto, Japan, 1956). An analysis of the electromyogram in blepharoptosis and nystagmus is also made in this report. (14 figures, 8 references) Yukihiro Mitsui.

Kinoshita, J. H. and Masurat, T. **Studies on the glutathione in bovine lens.** A. M. A. Arch. Ophth. 57:266-274, Feb., 1957.

This is a study of the known high concentration of glutathione in the lens and the factors that influence its activity there. (3 figures, 5 tables, 23 references)

G. S. Tyner.

Llorca, J. P. and Geniz Galvez, M. **Histologic changes observed in experimental cyclodialysis.** Arch. Soc. oftal. hispano-am. 36:545-549, June, 1956.

The authors report an experimental study on rabbits to demonstrate the structural changes produced by cyclodialysis, and to determine whether the hypotension produced by cyclodialysis is caused by a mechanical communication of the anterior chamber with the suprachoroidal space, or whether it is due to changes in the ciliary body on a vascular and nervous basis. Ten rabbits were operated upon by Heine's technique and killed on the 10th, 16th, 20th, 26th, and 30th day postoperatively and the eyes were examined histologically. The changes described and illustrated with photomicrographs support the contention that the operation produced an atrophy of the iris and ciliary body which was caused by interference with innervation. The possibility of a mechanical action is not excluded. (4 figures)

Ray K. Daily.

Lucas, D. R. and Newhouse, J. P. **The effects of nutritional and endocrine factors on inherited retinal degeneration in the mouse.** A. M. A. Arch. Ophth. 57:224-235, Feb., 1957.

Attempts were made to modify the course of a recessively inherited dystrophy of the visual cells of the mouse retina by administering large doses of various agents, including vitamins, hormones, amino acids, and intermediates of carbohydrate metabolism, to the animals, beginning shortly after birth. Only undernutrition and n-propylthiouracil were found to delay the course of dystrophy. (6 figures, 3 tables, 43 references)

G. S. Tyner.

Myers, Ronald E. **Function of corpus callosum in interocular transfer.** Brain 79: 358-363, 1956.

The author states that cats whose optic chiasm has been severed longitudinally are able to transfer learned visual responses from one side to the other. He feels that this occurs via the corpus callosum. Therefore both the optic chiasm and the corpus callosum were divided surgically in a series of cats. After this procedure there was a definite loss in the ability to transfer visual recognition from one eye to the other. The author feels that this demonstrates the role of the corpus callosum in interocular transfer. He also points out that such a loss has not been demonstrated in man with callosal injury or agenesis. (1 figure, 1 table, 13 references)

David Shoch.

Numao, C. **The relation of protein metabolism to retinal pulse wave and cerebral circulation.** Acta Soc. Ophth. Japan 60:1757-1764, Nov., 1956.

The protein metabolism, renal function and retinal pulse wave were studied in patients without actual hypertension in whom fundus findings characteristic of Keith-Wagener Stage III were recognized. The findings were no different from those in subjects with actual hypertension. Compared with normal controls of the same age group, there was a reduction in serum-albumin, and in renal blood

flow. By the analysis of the cornea pulse wave, a decrease in the "clinical resistance" and an increase in the "clinical rigidity" was found. (10 figures, 3 tables, 8 references) Yukihiko Mitsui.

Okuda, M. **Influence of ultrasonic radiation on the temperature of the eye.** Acta Soc. Ophth. Japan 60:1726-1733, Dec., 1956.

An ultrasonic wave of 5 w/cm² was applied to the eye of living or dead rabbits. In dead animals the temperature of the conjunctiva increased 4 to 5°C after five to ten hours' application. A lower increase in the temperature was observed in the aqueous, vitreous, retrobulbar tissue and lacrimal gland in the order given. In living animals, the order was aqueous, conjunctiva, vitreous, lacrimal gland and retrobulbar tissue from high to low. The degree of the temperature rise was much the same as in dead animals. (5 tables) Yukihiko Mitsui.

Orlowski, W. J. and Wekka, Z. **The hydrogen ion concentration of the aqueous in eye burns.** Klinika Oczna 26:117-126, 1956.

The authors discuss the literature on the penetration of alkali into the eye tissue. In order to investigate the problem they first examined the pH of normal aqueous in 23 rabbits, then burned the eye by the application of a normal solution of sodium hydroxide for one minute. The aqueous was collected at different intervals, and its pH was determined. The authors found that prompt removal of the caustic agent by washing is essential. Higher concentration of OH ions was found in the aqueous after longer exposure to the caustic agent. Paracentesis of the anterior chamber within three to five hours after exposure is advised; it may be even done in the first 24 hours but is of no use later. Repeated paracentesis is considered useless. (1 figure, 3 tables, 8 references) Sylvan Brandon.

Orzalesi, F. and Miglior, M. **The possibility of causing cataracts in the rabbit by means of electropositive protein.** Boll. d'ocul. 35:5-20, Jan., 1956.

In in vivo studies on the rabbit, the authors found that intravitreal inoculations of electropositive proteins resulted in the formation of a cataract of the complicata type. (3 figures, 8 references)

William C. Caccamise.

Pirodda, A. **The pH of human aqueous humor in senile cataract and in some forms of cataract complicata.** Boll. d'ocul. 35:229-237, March, 1956.

The author has studied the hydrogen ion concentration in the aqueous humor in cases of senile cataract, cataract complicata associated with Fuchs' heterochromia, cataract complicata associated with retinitis pigmentosa, cataract complicata associated with degenerative myopia, and cataract complicata associated with ablatio retinae. An abnormal pH was found only in cataract complicata associated with high myopia. In this condition there was a decrease in the pH. (2 tables, 16 references) William C. Caccamise.

Quintieri, C. **The action of sodium tetrachloroiodide in experimental herpetic keratitis of the rabbit.** Boll. d'ocul. 35:146-150, Feb., 1956.

The effect of sodium tetrachloroiodide in experimental herpetic keratitis in the rabbit was studied by the author. Local application of this chemical was found to modify the course of the herpetic keratitis. However, the author concludes that his experiments did not give very convincing results. (7 references)

William C. Caccamise.

Salgado, Gomez, E. and Fernandez Gonzalez, A. **Muskurelax in ocular surgery.** Arch. Soc. oftal. hispano-am. 16:761-770, Aug., 1956.

This muscle relaxing agent is known commercially as Muskurelax My-301. Its

chemistry, pharmacology, toxicity, antidotes, dosage and indications are discussed in detail. Its merits in ocular surgery are that it brings about perfect immobility of the globe, and ease of ocular manipulation by the surgeon—a perfect state of the muscles and vitreous. It has no effect on the intrinsic ocular musculature; some mydriasis is attributed to the hypotony which is caused, as in the case of curare, by a loss of vascular tone with improved venous circulation. In clinical doses this drug does not affect the respiratory rhythm, and does not produce laryngospasm or bronchospasm, as curare does; it does not affect the alveolar carbon dioxide content and carries no danger of asphyxia. For this reason the authors regard it as the agent of choice for obtaining muscular relaxation without respiratory paralysis. The dosage required for ophthalmic surgery is not toxic. For akinesis and retrobulbar injection the authors use 5 cc. of the solution administered 2 cc. each minute, five minutes before beginning surgery. The average dose is 2 cgm. per kilo of body weight.

Ray K. Daily.

Scassellati-Sforzolini, G. **A clinical and surgical consideration of Leber's disease: four cases with a finding of opticochiasmal arachnoiditis.** Riv. oto-neuro-oftal. 31:491-518, Nov.-Dec., 1956.

The author presents an excellent review of the literature concerning the relationship between Leber's disease and opticochiasmal arachnoiditis and describes four cases of Leber's disease in which exploratory craniotomy revealed an opticochiasmal arachnoiditis. He emphasizes that such patients require complete clinical and cisternographic study. Surgery may have a successful result only if it is carried out early in the course of the disease. The author questions the accuracy of the explanations of Leber's disease as hereditary. (8 figures, 47 references)

William C. Caccamise.

Sery, T., DevPaul, S. and Leopold, I. **Novobiocin, a new antibiotic.** A. M. A. Arch. Ophth. 57:100-109, Jan., 1957.

This study was undertaken to determine whether the antibiotic Novobiocin can penetrate into the chambers of the eye of experimental animals and how well it can be tolerated by ocular tissues. In the rabbit, it did not appear to enter the vitreous by any of the routes used except subconjunctival injection, and then only when toxic doses were used. The drug can be considered to have its greatest effectiveness against external ocular infections and those involving the anterior segment of the eye. (6 tables, 24 references)

G. S. Tyner.

Sommer, Siegmund. **Experiments on the effect of some industrial solvents on animals' eyes.** Klin. Monatsbl. f. Augenh. 130:105-110, 1957.

Rabbits were exposed for six weeks to the vapors of some of the organic solvents used in industry. Ethyl acetate caused an irritation of the conjunctiva, exposure to butanol was followed by superficial corneal lesions and butyl acetate caused a conjunctival irritation and at higher concentrations damage to the corneal epithelium. Cellosolve (ethylene glycoll monoethyl ether) did not cause any damage. (1 table, 8 references)

Frederick C. Blodi.

Stagni, S. **Variations in the permeability of the blood-aqueous barrier during fever therapy.** Boll. d'ocul. 35:503-509, July, 1956.

The author investigated the effect of fever therapy on the permeability of the blood-aqueous barrier to fluorescein (using the technique of Amsler and Huber) in 10 patients with various types of intraocular disturbance. An increased permeability was found in patients after fever therapy. (2 figures, 19 references)

William C. Caccamise.

Vodovozov, A., Lovlia, G. and Blank, N. **The local use of norsulphazol-sodium in ophthalmologic practice.** Vestnik oftal. 5:75-77, Sept.-Oct., 1956.

Norsulphazol-sodium was found to be more concentrated and more active than other sulpha preparations. It was tried on rabbits in 10- and 20-percent solutions; there was no irritation of the tissues of the eye of the rabbit. This preparation was also used on 30 patients of whom 10 had serpiginous ulcer of the cornea, 14 had purulent ulcer of the cornea and six keratoconjunctivitis. Instillation of a 20-percent solution every two to four hours in the affected eye was followed by improvement on the second to the fourth day. Epithelization of the cornea was observed on the fifth or sixth day and in some the hypopyon was absorbed by the fourth to the fifteenth day. (1 table)

Olga Sitchevska.

Wagner, Paul. **Experiments on the effect of some phenothiazine derivatives on the fundi.** Klin. Monatsbl. f. Augenh. 129:772-781, 1956.

A new phenothiazine Compound (NP 207, Sandoz) which is closely related to chlorpromazine was used for a while in psychiatric disorders. It was less toxic for the liver and less allergenic. However, many patients developed a pigmentary degeneration of the fundus with night blindness and field defects. The drug was given to rats, rabbits and dogs, but no ocular affection could be produced though a relatively high dosage was administered. (1 figure, 40 references)

Frederick C. Blodi.

Yanagida, H. **Permeability of conjunctival and dermal capillaries and blood-aqueous barrier in some ocular conditions.** Acta Soc. Ophth. Japan 60:1571-1574, Oct., 1956.

The Rumpel Leede test is apt to be positive in glaucoma, ocular tuberculo-

sis and after cataract surgery, showing an increase in the permeability of skin capillaries. However, the permeability of the blood-aqueous barrier as shown by the Amsler-Huber test does not necessarily increase in these conditions. (3 figures, 2 tables, 7 references) Yukihiko Mitsui.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Blois, Alcides S. **Aniseikonia.** Arq. brasil. de oftal 18:231-237, 1955.

Aniseikonia is defined. Symptoms are asthenopia, headache, photophobia, difficulty in reading, nausea, nervousness and diplopia. Routine therapy is not successful in relieving these symptoms, but adjustment in the size of the images may afford relief. The disparity may be total or meridional. Small differences between the two eyes are common, occurring in all of the patients examined in this study. In no instance was the difference greater than 1.5 percent in emmetropic individuals. It is believed that a 5-percent disparity in the retinal images is the maximum compatible with binocular vision.

It is emphasized that unexplained asthenopia in a patient who has emmetropia and orthophoria may be the result of aniseikonia, and that routine ophthalmological examination in such instances calls for the eikonic investigation. (14 references)

James W. Brennan.

Chmilevitch, A. **Practical notes on the method of skiascopy.** Vestnik oftal. 6:27-29, Nov.-Dec., 1956.

As the title indicates, a few practical remarks on the correct findings and avoidance of errors in skiascopy are given by the author. His remarks are chiefly concerned with skiascopy in patients without cyclopegia. Olga Sitchevska.

Corcostegui Moliner, Angel. **Surgical treatment of astigmatism.** Arch. Soc. oftal. hispano-am. 16:750-760, Aug., 1956.

The literature is reviewed. From experimental studies on rabbits, extending over a period of two years, using combinations and modifications of the various procedures advocated, the author concludes that a complete superior semicorneal limbic keratotomy with a conjunctival suture produces the greatest amount of hypermetropia. The danger of iris prolapse makes this operation impractical. A corneal suture closing the incision reduces the effect to one fourth. Incisions of 90 to 100 degrees without a suture produce an approximate corneal flattening of 2.5 diopters, and the effect on the corneal curvature of a 60-degree incision is negligible. An additional incision at the opposite end of the same meridian increases the effect somewhat. There is a greater flattening of the cornea from an operation at each end of the vertical than from the ends of the horizontal meridian. Sato's operation gave better results than a perilimbal keratotomy. The author reports three carefully selected cases in which three different techniques were used. He found that the various techniques for opening the anterior chamber in a meridian parallel to the meridian of least refraction are effective for the correction of moderately high myopic and mixed astigmatism. The refractive error in cases of anisometropia, in which lenses are not tolerated, may be reduced by surgery to a degree at which lenses can be tolerated, and binocular vision developed by orthoptic training. The reduction of refraction in the meridian of greatest refraction is greater the larger the amplitude of the keratometries, the more tangential the incision is to the cornea, and the closer it is to the pupil. The hypermetropic effect is more marked if the meridian of greatest refraction is vertical. A corneal suture protects against iris prolapse, but it reduces considerably the effect. The tendency of the cornea to recover its original form must be kept in mind, and a hyper-

correction aimed at. The effect of operations on the corneal surface is negligible. (25 references) Ray K. Daily.

Dieterle, P. and Gordon, E. **Standard curve and physiological limits of dark adaptation by means of the Goldmann-Weekers adaptometer.** Brit. J. Ophth. 40: 652-655, Nov., 1956.

The mean (standard) curve and its superior and inferior fiducial limits at a probability of 90 percent for dark adaptation measured with the Goldmann-Weekers adaptometer is given. The statistical method employed is based on an arithmetical mean of the logarithms of the logarithms of the threshold (log log threshold). This curve can be used as an exact basis for the measurement of adaptation, under similar conditions of examination, that is monocular examination with a cycloplegic pre-adaptation in twilight for 15 minutes followed by light adaptation of 1,400 apostilbs for 5 minutes. Dark adaptation is tested immediately with a test object of 100 percent contrast eliminated by a maximum starting light of 6 lux. (1 figure, 6 references)

Authors' summary.

Hill, Robert W. **The hyperbolas of accommodation and convergence.** A. M. A. Arch. Ophth. 57:259-265, Feb., 1957.

Convergence and accommodation have the same mathematical solutions (equilateral hyperbolas) when convergence is expressed in prism diopters. (3 figures, 3 references) G. S. Tyner.

Manzitti, E. and Paris, V. M. **Remarks on the development of vision.** Arch. argent. de pediat. 45:352-356, May, 1956.

The main phases of visual development are listed, both in the premature and in the full-term infant. Light sensitivity, color awareness, motor coordination and reflex conditioning are briefly discussed, emphasis being laid upon the possible

clinical applications of an exact knowledge of the ontogenetic timing.

A. Urrets-Zavalía, Jr.

Marin-Amat, M. **The physiological variations of the corneal curvature during life; their significance in ocular refraction.** Bull. Soc. belge d'opht. 113:251-293, June, 1956.

The physiologic variations in the curvature of the cornea during life are not only of scientific interest but are also of great practical importance; nevertheless a comprehensive investigation of the contributing factors in these changes has not been made. The present study was undertaken to furnish the necessary information. The work was divided into two parts. The anatomic characteristics of the cornea in diverse vertebrates and the causative agents in the determination of the corneal curvature, namely, the effect of the lid muscles, the inherent corneal elasticity, the effect of the extrinsic eye muscles, the possible action of the ciliary muscle and the particular distribution of the blood and lymph channels around the limbus are discussed in the first part. In the second part 17,881 refractions are reviewed, to decide on the possible changes in the kind of astigmatism. Every patient had an examination with the ophthalmometer. In about 83 percent a typical modification in the anterior corneal curvature was found. The cornea was spherical during infancy, showed a direct astigmatism during childhood and adolescence, again became spherical in adulthood and finally showed an astigmatism against the rule in old age. These distinctive events in corneal astigmatism were ascribed to diminishing tonus of the orbicularis muscle, the increasing strength of the internal rectus muscle during life, and to a certain nutritional deficit in the vertical meridian dependent on the arrangement of the lymph channels around the cornea. (2 tables, 10 references)

Alice R. Deutsch.

Raubitschek, E. **The arrow test for astigmatism.** Klin. Monatsbl. f. Augenh. 129:814-822, 1956.

This test, originally devised by the author, is here described in the form advocated by Pascal. It can also be used in combination with the new crossed cylinder arrangement. (Astikorrekt). (1 figure, 13 references) Frederick C. Blodi.

Salgado Gomez, E. **Indications and contraindications for scleral resection in myopia.** Arch. Soc. oftal. hispano-am. 16:771-776, Aug., 1956.

The literature is reviewed with special emphasis on the development of myopic refraction. The author advocates a scleral resection for malignant myopia, and in cases of high myopia in which Fukala's operation has been performed. In the absence of the lens the scleral resection serves as a prophylactic measure against retinal detachment. Ray K. Daily.

Yonemura, D. and Nango, R. **Strength duration of electrical stimulation in Oguchi's disease.** Acta Soc. Ophth. Japan 60:1733-1736 Dec., 1956.

In the completely dark or light adapted condition the strength-duration relationship in Oguchi's disease is normal. During dark adaptation, however, there is a definite delay in the voltage-threshold increase in Oguchi's disease. It has been shown by this study that the abnormality in Oguchi's disease is chiefly in the course of dark adaptation and not in its final status. (2 figures, 1 table, 7 references)

Yukihiko Mitsui.

5

DIAGNOSIS AND THERAPY

Ambos, E. **Foreign body localization with a contact glass of the suction type.** Klin. Monatsbl. f. Augenh. 130:37-44, 1957.

Four small iron spikes are attached to the contact glass. They guarantee the

marking on the film and cause wounds on the cornea which can be stained and used for orientation in the following operation. On the apex of the glass is a hollow metal rod, 20 mm. long. This is the length of the standard eye and can be used on the film as a scale. No calculations are necessary. The metal rod can also be used to fixate the eye, to exert certain movements for constructing the center of rotation and to pull the eye out of the orbit to improve the technique for a bonefree film. (6 figures, 11 references) Frederick C. Blodi.

Arkin, Wiktor. **Use of simplified Gullstrand's ophthalmoscope for fundus photography.** *Klinika Oczna* 26:245-248, 1956.

A short history of the photography of the eyegrounds is presented. Gullstrand's ophthalmoscope was used successfully; a Kine-Exacta camera was used in place of the ocular of the ophthalmoscope and a specially designed bulb (200 W. 24V.) was used. A transformer was used to dim the light for focusing and full light was used for exposure. Results were quite satisfactory. (7 figures, 7 references)

Sylvan Brandon.

Askovitz, S. **A note on the construction of the Schiötz tonometer.** *A. M. A. Arch. Ophth.* 57:7-10, Jan., 1957.

The author reports his mathematical investigation of the ideal shape for the contacting surface of the hammer assembly and concludes that it is the involute of a circle. (2 figures, 4 references)

G. S. Tyner.

Askovitz, S. I. **A fixation light for tonometry and tonography.** *A. M. A. Arch. Ophth.* 57:288-289, Feb., 1957.

For a target the author uses a streak retinoscope fastened to a stand and makes a sharp image on the ceiling at any distance by focusing with the sleeve of the retinoscope. (1 figure) G. S. Tyner.

Bernardczykowa, Anna. **Influence of acetylcholine on healing of eye burns.** *Klinika Oczna* 26:127-132, 1956.

The author used acetylcholine in second degree thermal and chemical burns of the eyes in 80 patients, first in the form of a 5-percent solution and later as a 2-percent ointment. Good results were obtained in 79 percent, satisfactory in 7 and poor in 12. It was noticed that under the influence of acetylcholine vascularization of the burned area was accelerated, necrotic tissue sloughed off faster and, particularly when used as ointment, the drug decreased the formation of adhesions and of corneal vascularization. It was not necessary to transplant buccal mucous membrane. Two cases are presented as examples. (1 table, 5 references)

Sylvan Brandon.

Binkhorst, C. D. and Flu, E. P. **Sterilization of intraocular acrylic lens prostheses with ultra-violet rays.** *Brit. J. Ophth.* 40:665-668, Nov., 1956.

Proper sterilization of the intraocular acrylic lens has been a problem and a cause of many of the complications. Heating and many of the chemical solutions deform the plastic. Ridley advocates immersion of the lens for one hour in cetrimide, an ammonium solution, but tests have shown that some of this solution is absorbed by the plastic which later causes an irritating iritis. The authors describe an instrument designed to expose the plastic lens to the bacteriocidal action of ultraviolet rays. With it one can eliminate all pathogens after 30 minutes exposure to 3,600 m. watt sec./sq.cm. This method has proved very satisfactory both in its bacteriocidal action and its lack of effect on the plastic material (2 figures, 1 table, 13 references)

Morris Kaplan

Breinin, Goodwin M. **Electromyography—a tool in ocular and neurologic diag-**

nosis. A. M. A. Arch. Ophth. 57:161-175, Feb., 1957.

I. Extraocular muscle electromyography provides a most useful test for the diagnosis and evaluation of therapeutic agents in myasthenia gravis. The best drug for this purpose is endrophonium (Tensilon chloride). (3 figures, 8 references)

II. Electromyography of the extraocular muscles has applications of interest in 1. neurogenic palsies of extraocular muscles, 2. progressive nuclear ophthalmoplegia, and 3. nystagmus. (17 figures, 9 references)

G. S. Tyner.

Cherednichenko, V. Fishing line as a suture material in plastic operations. Vestnik oftal. 6:32-33, Nov.-Dec., 1956.

A fishing line, "saturn," has been used in the Kharkov Eye Clinic as suturing material in operations on the skin of the lids. This particular fishing line is a smooth thread made of polyamide tar. It is not hygroscopic, is elastic, is stronger than silk or catgut. The thread causes no inflammation of the tissues and no scar remains after removal of the suture.

Olga Sitchevska.

De Alameida, A. Vaccination with BCG in ophthalmology. Rev. brasil. oftal. 15: 371-377, Dec., 1956.

The author believes that many of the uveal and retinal diseases are due to allergies and all of his patients are given a Mantoux test with 1:1000 tuberculin which should be read after 48 to 72 hours. Earlier readings will not be reliable. The author feels that the oral use of BCG vaccine in patients with positive Mantoux readings is very beneficial and never harmful in activating a tuberculous process. The administration of BCG in a total dose of 3.0 to 5.0 gm. does not produce any change in the anergic individuals and does produce some decrease in the amount of hypersensitivity of patients with a

positive Mantoux reaction. The author never was able to transform a positive reaction into a negative one, but feels that the eye lesions cleared more rapidly than could be expected without the BCG. (5 references)

Walter Mayer.

De Carvalho, Jose Siqueira. New developments in ocular therapeutics. Arq. brasil. de oftal. 19:1-5, 1956.

Therapy of ocular leprosy has advanced within the past several years with the introduction of the sulfones which have a chemotherapeutic effect against Hansen's bacillus. Subconjunctival injection of Promin (diaminodiphenylsulfone) in increasing doses causes regression of the keratitis, iridocyclitis and limbic nodules, with alleviation of the pain and improvement in vision. Systemic administration of sulfones in patients with leprosy apparently decreases the incidence of ocular complications. Prior to the use of this drug, surgical intervention in a leprosy eye was considered to be hazardous but now the author operates on such eyes almost daily for such conditions as cataract and glaucoma. In chronic cases the patients seem to derive benefit from extirpation of the lacrimal gland and infiltration of the site with the sulfone solution. It is known that Hansen's bacillus has a predilection for the anterior segment of the eye, which may account for the effectiveness of subconjunctival injection.

James W. Brennan.

Ferreira, Luiz Enrico. Examination of the fundus of premature infants. Arq. brasil. de oftal. 18:185-195, 1955.

The frequency of retrolental fibroplasia in premature infants makes it advisable for the ophthalmologist to be familiar with the technique of examining these small patients, and the findings of such examinations. The infant should be examined within the first two days of life and reexamined as often as necessary.

After preliminary external inspection, the pupils may be dilated with homatropine. The lids may be separated manually or by a speculum for ophthalmoscopy. Because of the frequency of myopia in pre-matures, retinoscopy is also recommended. An active infant may be pacified by a nipple with sugar water.

In this report, 39 infants were examined, 17 of whom were normal. Pallor of the nerve head was the most common abnormality. Pallor of the posterior pole and venous engorgement were second, followed by myopia. Turbidity of the vitreous, retinal edema, lens opacities and cicatricial masses were also observed. The possible relationship between oxygen administration and the development of retrolental fibroplasia is cited, referring to foreign investigators. (4 tables)

James W. Brennan.

Fison, T. N. **Herpes ophthalmicus.** *Lancet* 2:819-820, Oct. 20, 1956.

A case of severe herpes zoster ophthalmicus, hemorrhagic necrosis of the scalp area, perforation of the cornea and panophthalmitis with blindness, and a generalized hemorrhagic vesicular rash occurred in a 76-year-old man. There is a question as to whether herpes zoster can be disseminated or if a combination of herpes zoster and varicella existed in the same patient. (3 figures, 3 references)

Irwin E. Gaynon.

Foster, John. **Certain modifications in minor lacrimal instruments.** *Brit. J. Ophth.* 40:700-701, Nov., 1956.

Three modifications of lacrimal instruments are recommended. The lacrimal syringe cannula should be narrowed and shortened and made in a luer-lok base. The punctum dilater should have a second end with a very fine point for minute puncta. The lacrimal-duct probes should have grooved disc-shaped handles for better grasping. (3 figures)

Morris Kaplan.

François, J. and Verriest, G. **Conclusions from studies of the central scotopic visual field using Livingston's tests.** *Ann. d'ocul.* 189:605-610, July, 1956.

Having published several papers on scotopic campimetry, the authors attempt in this paper to summarize the conclusions which appear to them to remain valid. Scotopic campimetry may bring out field defects not apparent by usual methods of perimetry, particularly in the case of the following hemeralopigenic disorders: tapetoretinal degenerations; retinal separations (even after reattachment); senile macular degeneration; angioid streaks; hypertensive, diabetic and leukemic retinopathies; vascular occlusions; papilledema (which can be differentiated from pseudopapilledema from the onset); central serous choroiditis. Also in the case of localized macular affections, thanks to the existence of the normal scotopic central scotoma and pronounced isopteric gradients in the normal central scotopic field, minimal defects can be readily demonstrated. These considerations justify the recommendation that scotopic campimetry be widely employed in addition to photopic methods. The problems remaining to be solved relate mainly to improving the testing equipment. (13 references) John C. Locke.

Gaipa, M. **The Papanicolaou method in the diagnosis of tumors of the eye and its adnexa.** *Boll. d'ocul.* 35:491-502, July, 1956.

The author has used the Papanicolaou smear technique in the diagnosis of neoplasms in 57 patients with suspected tumors of the eye and its adnexa. In each case, a histologic follow-up study was made. The technique gave positive results in 36 cases of malignant tumor (16 cases of spindle-cell epithelioma, 6 of basal-cell epithelioma, 7 of malignant melanoma, 2 of retinoblastoma, 3 of lymphosarcoma of the orbit and 2 of probable

reticulohistiocytoma of the orbit). In only one case was there false positive. The author discusses cytological aspects of the neoplasms which he examined and also the validity and practicality of this technique. (16 figures, 1 table, 15 references)
William C. Caccamise.

Giggelberger, Hans. **Pathologic X-ray pictures of the sphenoid body.** *Klin. Monatsbl. f. Augenh.* 130:44-59, 1957.

Theoretically osteoporosis, osteolysis and hypertrophy can be distinguished. Practically all these forms frequently occur together.

The normal X-ray picture is first discussed and demonstrated on an isolated sphenoid. A few specific cases are illustrated. Chordomas of the sphenoid cause an intensive, but uncharacteristic destruction of the bone. Epitheliomas of the ethmoid cells may invade the sphenoid and cause osteolytic and osteoblastic changes. Eosinophilic adenomas of the pituitary may enlarge the sella but the osseous structure of the floor of the sella remains intact because of osteoblastic stimulation. Meningiomas of the sphenoid are characterized by hyperostoses in the area of the tumor and bony atrophy around it. (23 figures, 2 references)

Frederick C. Blodi.

Gil el Rio, E. and Hernandez Benito, E. **Wood's light in ophthalmology.** *Arch. Soc. oftal. hispano-am.* 16:777-794, Aug., 1956.

The literature is reviewed. (3 figures, 33 references)
Ray K. Daily.

Gordon, Dan M. **Hormonal-steroid therapy in ophthalmology.** *Tr. Pennsylvania Acad. Opth.* 9:113-116, 1956.

It is advisable to give fairly high dosages of a steroid until the patient has made an excellent response. Therapy should then be gradually tapered off, tak-

ing from one to two weeks to discontinue systemic therapy. Failure is usually caused by insufficient dosages for too short a time. Topical steroid therapy is indicated in diseases of the lids, conjunctiva, episcleral tissues, cornea, and in some cases of iritis. Systemic therapy is indicated in acute and chronic diseases of the uveal tract. ACTH is superior to the steroids in optic neuritis. Steroids may be combined with antihistamines where allergy is suspected. Irwin E. Gaynon.

Harper, J. Kennedy. **Anesthesia for intra-ocular surgery.** *Brit. J. Ophth.* 40: 661-664, Nov., 1956.

The author used general anesthesia and this was done in 160 cases because he found that local anesthesia was unsatisfactory for eye surgery. The patient was prepared 45 minutes before surgery with 100 mg. pethidine and 1/100 grain atropine. At surgery 10 mg. tubarine was given intravenously, followed immediately by 5-percent thiopentone. A pharyngeal tube for continuous flow of oxygen was inserted. Topical anesthesia was unnecessary. Relaxation of the eye was most satisfactory and the recovery phase was usually quiet and uneventful. Squeezing, restlessness, vomiting and pain were very rare and of no consequence. The average operating time was seven minutes, and 158 of the 160 operations were considered successful. (8 references) Morris Kaplan.

Hofmann, H. **The effect of muscle relaxants on the eye.** *Klin. Monatsbl. f. Augenh.* 130:32-37, 1957.

The well known effect of curare and succinylcholine on the extraocular muscles was tested on isolated human muscle.

A centrally effective relaxant (a glycerine-ether) was then tested and found to be of great help in the safe execution of intraocular operations. It makes an akinesia unnecessary and the eyeball remains soft. (23 references) Frederick C. Blodi.

Kleefeld, George. **The near-ultraviolet in ophthalmology.** Bull. Soc. belge d'opht. 113:293-307, June, 1956.

The significance of the use of near-ultraviolet light in clinical investigation and examination are discussed and several new devices using this type of illumination are described. (1 figure, 9 references)

Alice R. Deutsch.

Kopiec-Zaleska, Ewelina. **Hydrazide of isonicotinic acid in the treatment of ocular tuberculosis.** Klinika Oczna 26:165-170, 1956.

The author cites literature on treatment of tuberculosis of the eye with streptomycin, PAS and hydrazide of isonicotinic acid, with emphasis on the latter. Her own experience in 29 cases of various types of ocular tuberculosis is recorded. Treatment consisted of giving 5 mg. of hydrazide per Kg. three times daily but not more than 300 mg. per day for three to eight weeks. The drug was very well tolerated and caused nausea only in one case. When hydrazide was used alone only one patient of 13 was cured, six were improved and six were unimproved. The addition of streptomycin and PAS increased the number of definite cures. Out of 11 patients six were cured and five improved. Seven cases are presented in detail as illustrations. (2 tables, 19 references)

Sylvan Brandon.

Lincoff, H. and Cogan, D. G. **Unilateral headache and oculomotor paralysis not caused by aneurysm.** A. M. A. Arch. Ophth. 57:181-189, Feb., 1957.

The combination of unilateral frontal headache and oculomotor paralysis is often regarded as diagnostic of intracranial carotid aneurysm. However, the authors report nine examples of this syndrome, in three of which it was due to diabetes, in three to paraclinoid tumor, in one to leukemia, and in two to the entity called ophthalmoplegic migraine. (17 references)

G. S. Tyner.

Meyer-Schwickerath, G. **Photocoagulation of the ocular fundus and of the iris.** Ann. d'ocul. 189:533-548, June, 1956.

The phenomenon of phototraumatism due to watching an eclipse of the sun suggested that this effect of light might be used as a means of therapy. After several attempts the author succeeded in building an instrument with which he is able to create photocoagulations of the retina without opening the globe. The apparatus resembles a large ophthalmoscope and is equipped with a special lamp which emits only visible light and the shortest infrared wave lengths, other rays being eliminated by filters.

The fundus is first examined under reduced illumination. Then, with the beam directed at the retinal tear or other area to be treated, the intensity of the light is increased to a maximum. Retinal coagulations can be recognized as localized blanchings. Histologic examinations have shown that firm chorioretinal adhesions develop. Since adhesions cannot be achieved if the retina and choroid are separated by more than one diopter, the method has obvious limitations. Nevertheless, 27 cases of small localized detachments with peripheral tears were successfully treated by this method. In 23 detachments of a more extensive nature, the retina settled sufficiently after bed rest and binocular bandaging, and in another 14 cases, the technique was helpful as an addition to diathermy. Encouraging results were obtained in 41 cases of macular hole; although the photocoagulation destroyed a small area of central retina in some instances, the vision improved because of cure of a surrounding flat detachment.

Photocoagulation was used to prevent detachment in 28 eyes with peripheral degenerations of the retina, and in 11 eyes after detachment following a perforating injury of the globe.

It seemed to have some value in pre-

venting the recurrence of hemorrhages in retinal periphlebitis. Encouraging results were obtained in the treatment of two cases of early malignant melanoma of the choroid, and three cases of angiomas retinæ (v. Hippel-Lindau). The method was of no value in two cases of advanced retinoblastoma, but was successful in destroying a smaller growth, approximately the size of the disc.

The author has used the method successfully to produce an artificial pupil in an aphakic eye with seclusion of the pupil. It will not make a hole in a secondary membrane, but in cases where vascularization exists it might be helpful in sealing off blood vessels prior to discussion. (8 figures) John C. Locke.

Miller, J. M., Parke, D. W., Surmonte, J. A., Ginsberg, M. and Ablondi, F. B. **The use of the antibacterial drugs and streptokinase.** A. M. A. Arch. Ophth. 57: 241-244, Feb., 1957.

The combination of streptokinase and an antibacterial agent intramuscularly has shortened and improved the convalescence in patients who have had an enucleation of the eye. (1 reference) G. S. Tyner.

Mosquera, Jorge M. **Preliminary report on prednisolone therapy in acute ophthalmic conditions.** Arch. oftal. Buenos Aires 31:187-191, July, 1956.

Eighteen cases of assorted inflammatory conditions of the eye were submitted to the systemic administration of this new synthetic delta compound of cortisone, in daily doses of some 20 mg. The response was favorable in two instances of acute choroiditis, in six of acute and two of subacute iridocyclitis, in four of corneal abscess and in one case of corneal ulcer; in two other cases of corneal ulcer it was poor, as well as in one case of extensive lime burns of the conjunctiva and cornea.

A. Urrets-Zavalía, Jr.

Nelson, W. R. and Ng, E. **Radiographic interpretation in ophthalmology.** Tr. Pacific Coast Oto-Ophth. Soc. pp. 159-173, 1955.

Some of the common lesions in the orbit and their associated radiographic findings are described. Radiographic studies of the orbit should be stereoscopic, and one should know the principal orbital lesions. The ophthalmologist should give the roentgenologist an adequate history on and outline of the differential diagnosis. (28 figures, 7 references)

Lawrence L. Garner.

Norton, Herman J. **Data camera for labeling ophthalmic stereograms.** A. M. A. Arch. Ophth. 57:275-278, Feb., 1957.

A compact 35mm. film pack camera for permanent photographic labeling of individual ophthalmic stereograms is discussed. (4 figures, 1 reference)

G. S. Tyner.

Ogata, S. **Allergy of the eye with special reference to antibiotic allergy.** Acta Soc. Ophth. Japan 60:1643-1656, Oct., 1956.

This is a study of ocular allergy in 33 patients. Carbomycin, leucomycin, penicillin and streptomycin very often cause allergic manifestations such as conjunctivitis and blepharitis. Penicillin and streptomycin are apt to cause catarrhal conjunctivitis while the others are apt to cause follicular conjunctivitis. The period for sensitization is in the range of seven to 33 days.

A skin test by intradermal injection and an ocular test by the instillation of a suspected allergen are then studied. Ogata gives warning that anaphylactic shock may follow systemic administration, when an allergic reaction appears within a few minutes after application by instillation. The reaction is conjunctival hyperemia and chemosis. This test is harmless; without causing any systemic reaction it

is still very sensitive. A skin test in such individuals may cause a severe systemic reaction, even shock and should therefore be avoided. Ogata finally recommends an instillation into the eye of a drop of penicillin solution (100 U/ml) five minutes prior to a systemic administration. Most of the penicillin shock may be prevented by detecting anaphylactic persons in such a way. He also states that the sensitization by antibiotics does not disappear in the course of a few years. (5 figures, 1 table, 24 references)

Yukihiko Mitsui.

Pintucci, F. **Pre- and postoperative sedation in ocular surgery.** *Boll. d'ocul.* 35:135-145, Feb., 1956.

The author discusses the requirements of preoperative and postoperative sedation in ocular surgery. Emphasis in ocular surgery should be placed on akinesia of the ocular muscles, anesthesia of the ocular tissues, hypotension of the eyeball itself, physical and psychic relaxation of the patient, and inhibition of the vegetative nervous system. A preoperative "cocktail" consisting of largactil, fargan, antipar, and mephedine was found to be very effective. (25 references)

William C. Caccamise.

Prince, J. **A new slit-lamp color camera.** *A. M. A. Arch. Ophth.* 57:49-51, Jan., 1957.

A method of adapting a camera to the Haag-Streit slitlamp microscope is described. (3 figures, 2 references)

G. S. Tyner.

Rosas, Fernando E. **Localization of intraocular foreign bodies by roentgen examination.** *A. M. A. Arch. Ophth.* 57:245-249, Feb., 1957.

The method described was evolved for areas where other exact techniques are not available and requires only the usual X-ray machine and regular silk atraumatic

suture needles. (4 figures, 4 references)

G. S. Tyner.

Santalices Muniz, Faustino. **A new point for a corneal needle.** *Arch. Soc. oftal, hispano-am.* 16:697-699, July, 1956.

The author designed a new point for a corneal needle, which, he claims, makes its penetration easier and the corneal trauma less. The point is straight, 1.5 mm. in length, with a base of 2 mm. and triangular in section; it is flat in its inferior and convex in the superior surface. The needle is semicircular ending in an oval eye. (1 figure)

Ray K. Daily.

Schenk, H. **Akinesia of long duration.** *Klin. Monatsbl. f. Augenh.* 129:822-828, 1956.

Rhaetocain, a long-lasting local anesthetic, was used. The injection was given according to van Lint or O'Brien. Procaine was used in another series as control. The remaining orbicularis function was measured quantitatively. The muscle recovers in two hours after a procaine injection. Rhaetocain weakens the muscle for several days. It may cause an annoying edema. Its usefulness for certain operations and for blepharospasm is indicated. (4 figures, 10 references)

Frederick C. Blodi.

Schirmer, R. **The treatment of prethrombotic fundus hemorrhages.** *Klin. Monatsbl. f. Augenh.* 129:832-833, 1956.

The author advises the use of a horse-chestnut extract. It contains vitamine B₁ and is given intravenously. It seems to prevent a thrombosis of the central retinal vein. (1 reference)

Frederick C. Blodi.

Schupfer, F. and Carrai, P. E. **Intracarotid antibiotic therapy in endocular infections.** *Boll. d'ocul.* 35:65-76, Jan., 1956.

The authors present four cases of intraocular infection in which favorable re-

sults were obtained with intracarotid injections of penicillin and streptomycin. They used a solution of 500,000 units of penicillin with 250 micrograms of streptomycin which were dissolved in 10 cc. of a physiologic salt solution. (32 references)

William C. Caccamise.

Scott, Bryan O. **Effects of contact lenses on short-wave field distribution.** *Brit. J. Ophth.* 40:696-697, Nov., 1956.

With the increased wearing of lenses, it was decided to study the effect of these on short-wave applications. It was found that the contact lens interfered appreciably with the distribution of the short-wave heat to the eye and it is therefore recommended that contact lenses be removed from the eyes during short-wave application. (2 figures, 1 reference)

Morris Kaplan.

Sencer, Walter. **Lumbar puncture in the presence of papilledema.** *Mt. Sinai Hosp. J., N.Y.* 23:808-815, Nov.-Dec., 1956.

"The lumbar puncture is not a dangerous procedure in patients who have ophthalmoscopic findings which might indicate increased intracranial pressure. The lumbar puncture is of diagnostic value and the spinal fluid findings assist in managing such problems." (5 tables, 5 references)

Irwin E. Gaynon.

Shapiro, I. **Radioactive phosphorus in differential diagnosis of ocular tumors.** *A. M. A. Arch. Ophth.* 57:14-17, Jan., 1957.

The results of isotope countings in 24 pathologically proved cases in a series of 80 radioactive phosphorus determinations are reported. The author concludes that it is a valuable adjunct in diagnosing ocular malignancy but advises conservatism in its use. (12 references)

G. S. Tyner.

Silvan, Fernando. **A new model erisophake.** *Arch. Soc. oftal. hispano-am.* 16:795-802, Aug., 1956.

A new model of an erisophake is described. It has all the merits of the classical erisophake, and includes in addition the regulation of the degree of vacuum. The suction is manipulated by means of a foot pedal, relieving the hands of maneuvers required by the manually controlled erisophake. The development of the erisophake is reviewed (1 table, 17 references)

Ray K. Daily.

Sivasubramaniam, P. **Method of cutting lamellar grafts.** *Brit. J. Ophth.* 40:697, Nov., 1956.

Removing a lamellar graft from the intact eye presents no difficulties, but from an isolated cornea the procedure is difficult. It is recommended that a cork be trimmed to the curvature of the cornea and sterilized by boiling. The cornea is pinned to its surface and the graft easily removed. (1 reference)

Morris Kaplan.

Stockinger, L. and Schenk, H. **Akinesia of long duration.** *Klin. Monatsbl. f. Augenh.* 130:26-32, 1957.

This is the second part of a study on the use of a long-lasting local anesthetic (Rhaetocain) for akinesia. The sciatic nerve of rabbits was injected. The paresis lasted for 1 to 15 days. The nerve was resected after a varying length of time. The Marchi stain began to be positive 48 hours after the injection. The myeline disintegration started 72 hours after the injection, and resembled a toxic neuritis. (6 figures, 1 table, 6 references)

Frederick C. Blodi.

Stringham, J. **Pediatric anesthesia.** *A. M. A. Arch. Ophth.* 57:24-32, Jan., 1957.

This paper should be read in its entirety by ophthalmic pediatric surgeons for its many valuable suggestions. Preoperative medication is stressed. (12 figures, 6 references)

G. S. Tyner.

Tassman, I. S. **Significance of ocular changes occurring after middle age.** *Geriatrics* 11:493-502, Nov., 1956.

Brief descriptions are given of the common ocular abnormalities with notes on their recognition, management, and prognosis. First discussed are changes in the external eye and appendages: entropion, ectropion, xanthlasma, tumors, Sjögren's syndrome, corneal dystrophies, ulcers, and scleromalacia. Then changes in the structures of the inner eye are discussed: presbyopia, cataracts, glaucoma, vascular accident, diabetes, and senile degenerations. (7 references) Harry Horwich.

Thiel, H. L. **A fluorescent light for facilitating cataract extractions.** *Klin. Monatsbl. f. Augenh.* 130:116-117, 1957.

This is a rod-shaped light which can be used for extractions or discissions. This light was found to be harmless to the eyes of rabbits and guinea pigs. (1 figure)

Frederick C. Blodi.

Wagener, Henry P. **Amaurosis fugax: specific type of transient loss of vision.** *Illinois M. J.* 111:21-24, Jan., 1957.

Amaurosis fugax is defined as a transient blindness, usually unilateral, due primarily to a local interruption of blood supply to the retina rather than to a lowering of the systemic blood pressure. Wagener lists as the possible causes of this symptom: migraine (here the disturbance is usually of the occipital cortex with a resultant homonymous hemianopsia), spasm secondary to local lesions in the retinal vessels, spasm secondary to lesions of the carotid artery and finally insufficiency due to arteritis of a branch of the aorta (pulseless disease). The latter condition should be treated with cortisone; the other two entities are an indication for long term anticoagulant therapy. (20 references)

David Shoch.

Wilk-Wilczynska, Maria. **Value of different topical anesthetics in ophthalmology.** *Klinika Oczna* 26:133-152, 1956.

The author discusses the relative value of various topical anesthetics. She is particularly interested in the properties of cocaine which are described in detail. Cocaine is considered to be the best of the topical anesthetics. In usual solutions with addition of adrenalin it is not absorbed into the organism and does not cause any toxic symptoms. Microscopic examination of rabbits' eyes after application of 5 percent cocaine preoperatively or $\frac{1}{4}$ percent cocaine used five times daily for 12 days did not show any abnormalities. Slitlamp examination of human eyes also did not show any damage. The author feels that addition of $\frac{1}{4}$ percent cocaine to antibacterial eye drops is indicated. (3 figures, 6 tables, 21 references)

Sylvan Brandon.

Zekman, Theodore N. **Ophthalmologic use of new stereo attachment.** *A. M. A. Arch. Ophth.* 57:286-287, Feb., 1957.

A lens for three-dimensional close-up photographs has been designed as an attachment to the Exakta Model V or VX 35 mm. camera. The device is called the Kin-Dar hypostereo attachment. (1 figure)

G. S. Tyner.

6

OCULAR MOTILITY

Benchimol, R. **Treatment of convergent strabismus.** *Rev. brasil. oftal.* 15:421-436, Dec., 1956.

The author calls attention to the significance and importance of binocular vision and feels that treatment should be carried out at the earliest possible time, in order to prevent the establishment of amblyopia or anomalous correspondence. He discusses the surgical and orthoptic treatment of this type of strabismus. He presents six case histories, with refrac-

tive findings and measurements of muscle imbalance and treatment, accompanied by photographs of patients before and after the treatment which included surgery and orthoptic exercise. (13 figures, 23 references)
Walter Mayer.

Blatt, N. and Regenbogen, L. **Orthoptic management and operative indications in strabismus.** *Presse Med.* 65:22-24, Jan. 5, 1957.

The authors divide their cases of strabismus into two groups on the basis of the age of onset of the squint. If it appears before the age of three year surgery is performed as soon as reliable measurements can be made, usually within six months. If the squint appears after the age of three years orthoptic treatment is recommended for a minimum of three to five months. If there is no change with orthoptic exercises, surgery is indicated. The usual emphasis is placed on pre-operative occlusion for amblyopia. In addition to the standard operations for strabismus the authors perform many tenotomies of the medial rectus muscle because they feel that this is more likely to preserve good convergence.

With the use of pre- and postoperative orthoptics, successful cosmetic results have increased from 75 to 90 percent and successful functional results from 25 to 82 percent.
David Shoch.

Boeder, Paul. **An analysis of the general type of uniocular rotations.** *A.M.A. Arch. Ophth.* 57:200-206, Feb., 1957.

The author discusses Listing's law and the "false torsion" that occurs in oblique positions of the globe. (9 figures, 6 references)
G. S. Tyner.

Cramer, F. E. K., Puppo, J. B. and Corsellas, A. C. **Frequency and significance of convergence insufficiency.** *Arch. oftal. Buenos Aires* 31:117-124, April, 1956.

The signs and symptoms of this common disturbance of ocular motility are reviewed and discussed. Treatment must consist essentially of measures to improve fusion amplitude and to readjust the convergence-accommodation ratio by means of orthoptic measures, so that the positive portion of the relative convergence becomes larger than the negative. By these means the patient is brought to use that middle third of this function called by Percival area of comfort. One hundred consecutive asthenopic patients and 500 medical students were tested for the condition; 30 percent of the former and 18.4 percent of the latter presented some degree of the disturbance. As a rule, patients in whom the condition was very marked suffered less than those in whom it was of a moderate degree. (1 figure, 8 tables, 17 references) A. Urrets-Zavalía, Jr.

Ellis, G. S. and Haik, G. M. **Development of vision in the cross-eyed child.** *Louisiana St. M. Soc.* 108:450-454, Dec., 1956.

This is a short article concerned with the generalities of strabismus and directed at the pediatrician and general practitioner. It briefly covers mechanisms of vision (with a useful table on visual acuity at various ages), etiology, and treatment of crossed eyes. The authors correctly make a plea for initiation of therapy before the age of six years, if binocular vision is to result. (1 table, 3 references)
David Shoch.

Focosi, M. and Guzzinati, G. C. **The utilization of marginal myotomies in the correction of hyperfunction of the inferior oblique muscle.** *Boll. d'ocul.* 35:202-216, March, 1956.

The authors performed 33 operations in which marginal myotomy was carried out on the inferior oblique muscle. The results suggest that this procedure is indicated in those patients who have a slight

degree of over-activity of the inferior oblique muscle and in whom there is a favorable prognosis for the recovery of simple binocular single vision. (26 references)

William C. Caccamise.

Folk, E. **Superior oblique tendon sheath syndrome.** A.M.A. Arch. Ophth. 57:39-40, Jan., 1957.

A cure of superior oblique tendon sheath syndrome (as previously described by Brown) is presented. Simple stripping was ineffectual, but when combined with surgery on the inferior oblique muscle, the result was better, but not excellent. (4 references)

G. S. Tyner.

Guzzinati, G. C. and Cristiani, R. **The relationship of a vertical component in concomitant strabismus to the type of retinal correspondence.** Boll. d'ocul. 35: 21-42, Jan., 1956.

The authors compare the retinal correspondence in 154 patients with simple horizontal heterotropia, and 136 patients with a vertical imbalance. There was no significant difference in the incidence of abnormal retinal correspondence. (35 references)

William C. Caccamise.

Harcourt, J., Delmarcelle, Y. and Hainaut, H. **Poliomyelitis and paralytic squint.** Bull. Soc. belge d'opht. 113:464-472, June, 1956.

Disturbances of ocular motility have been described in about 5 percent of patients with poliomyelitis. Nystagmus, total and partial external and internal ophthalmoplegias, weakness of the facial nerve and affection of the cervical sympathetic have been found. The histories of seven patients are reviewed. Two patients had a paralysis of the sixth nerve, two had a paralysis of the seventh nerve with lagophthalmos, and one patient had a paralysis of the sixth and seventh nerves. The sixth patient had a paralysis of conjugate gaze. The seventh patient, the only

adult in this series, showed a paralysis of the internal rectus muscle. Weakness of ocular muscles may be the first symptom of poliomyelitis, although it manifests itself mostly with other signs and symptoms. Nearly all impairment of function of the external eye muscles is transitory; the paralysis of the conjugate gaze is more obstinate and may persist for life. However, the transformation of a paralytic squint into a concomitant one was observed. Such a change may occur rapidly after several weeks as well as after several months and seems to be dependent on the presence of anomalies of refraction. Paralysis of ocular muscles are seen in other virus diseases, such as lymphocytic meningitis, and virus diseases should be seriously considered whenever the etiology of paralytic squint is investigated. (3 figures, 10 references)

Hauser, P. J. and Burian, H. M. **Fixation patterns in strabismus amblyopia.** A.M.A. Arch. Ophth. 57:254-258, Feb., 1957.

Using the test advocated by Brock and Givner the authors found that this test did not give evidence that the majority of patients fixated eccentrically with their amblyopic eye. They did find, however, that a stronger stimulus was needed. (3 figures, 2 tables, 5 references)

G. S. Tyner.

McAuley, F. D. **Progressive external ophthalmoplegia.** Brit. J. Ophth. 40:686-690, Nov., 1956.

Progressive external ophthalmoplegia has generally been considered to be a muscular dystrophy rather than the result of a degeneration of the oculomotor nuclei. Four cases with bilateral ptosis and much restriction of ocular movement are reported. Two were in mother and daughter and several relatives had similar manifestations. Biopsy of other muscles of the body showed the disease to be a part of

generalized progressive muscular dystrophy. (7 figures, 15 references)

Morris Kaplan.

Mercado, Modesto A. **Chronic progressive ophthalmoplegia of von Graefe.** Arq. brasil. de oftal. 18:250-252, 1955.

A 17-year-old girl had bilateral ptosis and paralyzes of all the extraocular muscles. She had a resultant fixation of the eyes with limitation of gaze. The disturbance is ascribed to a progressive bulbar paralysis involving the motor nuclei of the eyes and sparing the intrinsic muscles. In the differential diagnosis myasthenia gravis and Wernicke's hemorrhagic superior poliomyelitis were considered. (6 figures, 3 references)

James W. Brennan.

Puglisi-Duranti, G. **Diencephalo-rachidian therapy in oculomotor paralyzes and pareses.** Riv.oto-neuro-oftal. 31:539-553, Nov., 1956.

The author advocates the treatment of oculomotor paralyzes and pareses with air insufflation into the cerebrospinal system. (6 figures, 19 references)

William C. Caccamise.

Sanna, M. **The etiology and the frequency of external ocular paralyzes.** Riv. oto-neuro-oftal. 31:425-447, Sept.-Oct., 1956.

The author presents a statistical analysis of 604 cases of paralysis of the external ocular muscles. Emphasis is placed on the frequency and the etiology as well as the age of the patients. The lateral rectus muscle was most frequently involved, the muscles supplied by the oculomotor nerve less often and the superior oblique muscle least. The ratio of male patients to female patients was 5 to 4. Trauma was the most frequent cause of paralysis in patients who were 20 to 50 years old. In older patients tumors and vascular conditions were the commonest cause and in younger patients paralyzes on the basis of en-

cephalopathy, toxic infections and congenital abnormalities were more frequent. (8 tables, 20 references)

William C. Caccamise.

Starkiewicz, Witold. **Localization method of squint treatment.** Klinika Oczna 26:153-160, 1956.

The author gives schematic plans for treatment of convergent squint of various kinds and in different age groups. Three basic procedures are used: correction of refractive error after complete atropinization, occlusion of the better eye and surgery. When using occlusion the author emphasizes the need of correlation of tactile stimuli with the visual stimuli by using the hands together with the eye in handling small objects and drawing. Alternating and partial occlusion are used in appropriate cases. Surgery can be repeated but no method is suggested. Additionally prisms may be used preoperatively to remove abnormal correspondence and postoperatively to facilitate fusion.

Sylvan Brandon.

Taylor, E. J., Shannon, T. E. and Stanworth, A. **Stereopsis and depth perception after treatment for convergent squint.** Brit. J. Ophth. 40:641-651, Nov., 1956.

Over a 10 year period, 263 patients were examined to determine what can be expected in improvement and what factors influence this improvement. The age of the patient had little bearing, whereas the age of onset of the squint and the length of time of correction after appearance of the squint had immediate and direct bearing on post-operative stereopsis. The greater the degree of binocular vision before the surgery, the greater the function afterwards. The results were likewise better in patients with eyes whose vision did not differ by more than two Snellen lines or 3 diopters in refraction. (6 tables, 16 references).

Morris Kaplan.

7

CONJUNCTIVA, CORNEA, SCLERA

Barraquer Moner, Joaquin. **Essentials of keratoplasty.** Arch. Soc. oftal. hispano-am. 16:728-741, Aug., 1956.

The essential requirements for a successful keratoplasty are thoroughly discussed. To be considered for complete organic tranquility are a twilight state of the patient, neurovegetative equilibrium, general akinesia and local anesthesia. Good closure of the incision is insured by regularity of the edges of the section of the receptor eye as well as the graft, and direct multiple sutures. Operation under microscopic control insures a perfect section in lamellar keratoplasty and correct placement of sutures. Minimal surgical trauma depends on a good technique and perfect instruments. Surgery in miosis affords better centration, a clean-cut section with the trephine, and less danger of synechia, hypertension and iris prolapse. (17 figures, 4 references)

Ray K. Daily.

Binder, R. F. and Binder, H. F. **Regenerative processes in the endothelium of the cornea.** A.M.A. Arch. Ophth. 57:11-13, Jan., 1957.

The authors' studies indicate that the regeneration of the corneal endothelium of the rabbit ordinarily occurs by amitosis. The cells with long nuclei noted during healing are macrophages. (4 figures, 11 references)

G. S. Tyner.

Blatz, G. **Corneal necrosis in measles.** Klin. Monatsbl. f. Augenh. 129:763-772, 1956.

In five children corneal necrosis was observed within two months at the University Clinic in Leipzig. All were girls and the age ranged from one and one half to five years. Only one child recovered with two useful eyes. Three children were left with dense corneal scars and one child died. The clinical picture resem-

bled keratomalacia but there was no vitamin A deficiency, nor was there a consistency in microorganisms found in the ulcer. It is possible that the measles virus itself lodges in the cornea. The condition resembles the inflammation of the middle ear and the drum after measles. (6 figures, 3 tables, 18 references)

Frederick C. Blodi.

Buesa Lorente. **Therapy of dendritic keratitis.** Arch. Soc. oftal. hispano-am. 16:684-693, July, 1956.

The author advocates local application of alcohol to the epithelial lesions, and reports 11 cases illustrating the beneficial results of this procedure. Of the antibiotics, aureomycin is most effective. Vitamins B₁, C and A combined with auto-hemotherapy are useful. (54 references)

Ray K. Daily.

Christensen, Leonard. **Cornea and sclera.** A.M.A. Arch. Ophth. 57:295-310, Feb., 1957.

This annual review considers corneal injury and repair, keratoplasty, infections, medical therapy, and the sclera. (133 references)

G. S. Tyner.

D'Ermo, F. **A case of perforating scleromalacia.** Boll. d'ocul. 35:191-201, March, 1956.

The author describes a case of perforating scleromalacia which he observed in a woman with severe generalized arthritis. The classification and the literature concerning this group of rare scleral lesions are reviewed. In the author's case a treatment which included the use of cortisone and plasma transfusions was completely ineffective. (1 figure, 41 references)

William C. Caccamise.

François, J., Gildemyn, H. and Rabaey, M. **Cancerous melanosis of the cornea.** Ann. d'ocul. 189:496-504, May, 1956.

The authors present clinical and histo-

pathologic findings in a case which they believe corresponds to Reese's cancerous melanosis. They consider the lesion unusual in having originated in normal cornea (there was no preëxisting nevus) and in being confined entirely to the cornea (other than dilatation of the vessels, there was no associated abnormality of the conjunctiva). Subconjunctival injections of acetylcholin were of no benefit. A good result was obtained with simple local excision. (7 figures, 18 references)

John C. Locke.

François, J., Rabeay, M. and Evans, L. **Epithelial tumors of the conjunctiva.** Bull. Soc. belge d'opht. 113:436-46, June, 1956.

The diagnosis of conjunctival epithelial tumors is not easy and often deceiving; an exact clinical and pathological examination and a detailed history are essential. The authors recognize 1. simple hyperplasia, 2. hyperplasia papillomatosa (benign and malignant), 3. epithelioma intra-epithelialis, and 4. epithelioma spino-baso-cellularis. Fifteen cases of conjunctival epithelial tumors are discussed in detail. The excision of this type of tumor is not difficult and the results are mostly good but recurrences are described. Diathermy coagulation and excision also gave satisfactory results. Beta irradiation is advised only for very small tumors. The treatment of choice of the authors is contact X-ray therapy. They use a Metalix Phillips-tube, a tension of 50 kilovolts and 2 milliamperes at a distance of 40 mm. surface lead and no filter, doses 5000 to 6000 r, and 10 to 12 sittings either daily or every other day. In spite of the short active distance in contact irradiation, an occasional injury to the deeper structures, especially to the lens, is possible. No complication of the X-ray treatment however was noticed in the series discussed. In all cases the recovery was speedy and complete. (25 figures, 37 references)

Alice R. Deutsch.

Frezzotti, R. **Talcum granuloma of the bulbar conjunctiva, a rare occurrence in ophthalmology.** Boll. d'ocul. 35:345-351, May, 1956.

The author discusses the case of a 12-year-old girl who developed a hyperplastic lesion of the bulbar conjunctiva of the right eye. One month previously a "dermoid cyst" had been removed from this same area. (5 figures, 8 references)

William C. Caccamise.

Gramberg-Danielsen, B. **Blood staining of the cornea.** Klin. Monatsbl. f. Augenh. 129:828-831, 1956.

A nine-year-old boy developed blood staining of the cornea after trauma. Twice surgery was attempted because the disc-shaped opacity was mistaken for a luxated lens. The eye was finally enucleated because of secondary glaucoma. (1 figure, 14 references)

Frederick C. Blodi.

Hermanns, M. R. **Bandshaped keratopathy and ichthyosis.** Bull. Soc. belge d'opht. 113:316-327, June, 1956.

The case history of a 55-year-old man with a bilateral primary bandshaped keratopathy is reviewed. The fluorescein test was negative. There were no other signs of ocular abnormalities. The patient, however, had a localized ichthyosis. The calcium content of his plasma was normal, cholesterol was 342 mg. He was given high doses of vitamin A (150,000 units daily) to which 15 mg. of vitamin E was added after a few weeks. He also used a 1-percent vitamin A ointment locally. As long as this treatment was continued, a considerable improvement of the skin and eye occurred and the plasma cholesterol dropped to more nearly normal values. Later a recurrence of the disease was treated with heparin and local vitamin A palmitate. Local treatment of the cornea was avoided in order to demonstrate a certain dependence of the corneal disease on the skin disorder. (1 figure)

Alice R. Deutsch.

Holland, R. W. B. **The treatment of trachoma with subconjunctival injections of chloramphenicol.** A.M.A. Arch. Ophth. 57:214-217, Feb., 1957.

The combined oral and local administration of chloramphenicol has been shown to be effective in the treatment of trachoma. This, however, is impractical for most patients in Pakistan. Subconjunctival injections were therefore resorted to with good results, although they caused considerable discomfort. The length of treatment and the cost was much less.

G. S. Tyner.

Kalinin, A. **Keratoplasty in the Kopisk City Hospital.** Vestnik oftal. 5:82-84, Sept.-Oct., 1956.

During the years 1952 to 1954 eleven keratoplasties were done in ten patients. Partial penetrating keratoplasty was done in nine, subtotal penetrating in one and partial lamellar keratoplasty in one. The author used Filatov's trephine and used only four sutures; a conjunctival flap was used in six patients, a cellophane membrane in four and an egg membrane in one. The material for keratoplasty was taken either from the cadaver's cornea or from infants who died from asphyxia. The time of the conservation of the cornea was 72 hours. Four transplants were transparent and seven opaque; the latter were used when the keratoplasty was done for cosmetic purposes. The complications are enumerated. (1 drawing, 1 table)

Olga Sitchevska.

de Magalhães, Paulo Braga. **Erosive ectodermoses of external mucous membranes.** Arq. brasil. de oftal. 18:181-184, 1955.

This syndrome is characterized by a varicelliform or purpuric cutaneous eruption associated with inflammation of various mucous membranes (conjunctival, nasal, bucco-pharyngeal, anal, preputial). The clinical picture begins with conjunc-

tivitis or stomatitis, rapidly followed by a generalized erythematous cutaneous eruption. The genitals are involved in about 25 percent of the cases, and the digestive tract and respiratory systems in a smaller percentage. Hemorrhagic crusts develop from vesicles which appear on the skin within a week of onset.

The conjunctivitis is catarrhal at the onset, becoming mucopurulent through secondary infection. Small vesicles are formed which rupture, forming ulcers. Corneal ulcers, uveitis or corneal perforation may also occur. In some instances a membranous conjunctivitis may be observed. Loss of vision may result from corneal vascularity. The clinical picture of keratoconjunctivitis sicca may be produced in severe cases.

The following may be considered as examples of this syndrome: Stevens-Johnson's syndrome, exudative erythema of Helbra, Behçet's syndrome, and Reiter's syndrome.

James W. Brennan.

Moss, J. **Method of removing wooden splinters from the cornea.** Brit. J. Ophth. 40:698-699, Nov., 1956.

A rather large wooden splinter perforated the cornea and protruded into the chamber just short of the lens. It was allowed to remain there for three months, when it was decided that it must be removed. One wide keratome was introduced just anterior to the lens to prevent damage while a smaller one was used to make a section over the splinter which was then removed easily. Healing was uneventful. (1 figure, 1 reference)

Morris Kaplan.

Pintucci, F. **Irradiation with heat in herpetic keratitis.** Boll. d'ocul. 35:485-490, July, 1956.

The author points out that there is no form of therapy commonly employed in the treatment of herpetic keratitis that

has a direct effect upon the herpes virus. He then reports the results that he obtained in 166 cases of superficial herpetic keratitis in which the lesion was treated with heat irradiation. The results have been most satisfactory, and the author feels that this is the treatment of choice in cases of superficial herpetic keratitis. Recently he has combined the heat irradiation with a lysozyme collyrium. The latter apparently has a protective action on the corneal epithelium that is not yet involved in the herpes virus. (1 figure, 19 references)

William C. Caccamise.

Schmid, Ernst. **A corneal disease of furniture finishers.** *Klin. Monatsbl. f. Augenh.* 130:110-115, 1957.

These corneal lesions (superficial, small vacuoles) are caused by the solvent. They occur also in other industries (lacquer, straw hats, celluloid, beads). Many of these patients were observed. The disease is more frequent in winter when the plants are heated and poorly ventilated. The prognosis is good. Similar corneal lesions could be produced in cats. Especially injurious was xylol. (1 figure, 12 references)

Frederick C. Blodi.

Sobel, G., Aronson, B., Aronson, S. and Walker, D. **Pharyngoconjunctival fever: report of an epidemic outbreak.** *A.M.A. Dis. Child.* 92:596-612, Dec., 1956.

An outbreak of this rather novel syndrome is described. It occurred in two isolated portions of a boys' summer camp and consisted of two phases. First there was a rather scattered outbreak of quite mild complaints; then, about a month later, an explosive epidemic broke out with some features so severe that poliomyelitis was considered in the differential diagnosis. The numerous signs and symptoms are described in detail, the most important being fever, adenopathy, upper respiratory inflammation, abdominal com-

plaints, malaise, and conjunctivitis. Conjunctivitis occurred in 80 percent of the patients. Viral studies were performed for corroboration and were positive. (7 figures, 3 tables, 23 references)

Harry Horwich.

Tosti, E. **Protection of the cornea with severe keratitis with lagophthalmos in a case of temporarily inoperable cicatricial ectropion.** *Boll. d'ocul.* 35:465-470, July, 1956.

The author discusses a case of lagophthalmos resulting from cicatricial ectropion and complicated by severe keratitis and incipient endophthalmitis in an 18-months-old patient. The author emphasizes the difficulty in treating such cases of keratitis, and he describes his surgical method which gave favorable results. The surgery consisted essentially of a bridge flap of tarsal conjunctiva which extended over the involved cornea from the inferior fornix to the superior fornix. (7 figures)

William C. Caccamise.

Van Horne, R. G. **An intrafamilial epidemic of pharyngo-conjunctival fever.** *Arch. Int. Med.* 99:70-73, Jan., 1957.

APC virus type 3 was isolated from three members of a family of seven who were suspected of having this condition. A fourth member showed a rise in titer without isolation of virus. These four had conjunctivitis, and the virus was isolated from the conjunctiva in the first three members. The remaining three members had symptoms without viral corroboration. (7 references)

Harry Horwich.

Weerekoon, Lloyd M. **Epidemic keratoconjunctivitis in Ceylon.** *Brit. J. Ophth.* 40:691-695, Nov., 1956.

Epidemic keratoconjunctivitis is rather wide-spread in Ceylon and an occupational disease since it occurs commonly in paddy workers who get splashes of the

muddy water into their eyes. In Ceylon it is a blinding disease. It follows a definite pattern of moderate conjunctivitis followed by fine keratitic spots and some loss of vision. The eye then becomes white and opacities of the cornea develop and progress to complete opacification of the corneas. If treatment with aureomycin and terramycin is instituted early and is persisted in, the condition clears promptly. (4 tables, 16 references) Morris Kaplan.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Boeri, R. and Frera, C. **Sympathetic heterochromia**. *Riv. oto-neuro-oftal.* 31: 554-561, Nov.-Dec., 1956.

The authors review the literature concerning heterochromia particularly as it pertains to so-called sympathetic heterochromia. They then discuss their findings in 225 patients with neurologic or surgical lesions of the centers or pathways of the cervical part of the sympathetic system; 102 of these patients manifested gross signs of sympathetic disturbance. Only two of the patients had heterochromia and both had syringomyelia. In no case of a traumatic or surgical lesion of the cervical sympathetic system of an adult or an infant was there heterochromia. Syringomyelia is considered to be a form of congenital dysplasia. (1 table, 38 references)

William C. Caccamise.

Christensen, L. and Rowen, G. E. **Diagnosis of malignant melanoma by subretinal fluid studies**. *Tr. Pacific Coast Oto-Ophth. Soc.* pp. 175-183, 1955.

Studies of subretinal fluid were made using the Papanicolaou technique to identify the tumor cells in the subretinal fluid. Although cells are found in malignant melanoma, often a positive diagnosis is very difficult because of the extreme difficulty of differentiating tumor cells

from histiocytes. When the pigment epithelium is disturbed some of the pigment cells migrate into the subretinal space where they appear as large round cells with or without pigment and assume the role of macrophages. The differentiation of tumor cells from these pigment cells is at times impossible. When samples of subretinal fluid were taken by means of a penetrating diathermy needle, extension of the malignant melanoma through the puncture wound was noted; the procedure cannot be recommended for diagnosis. (6 figures, 8 references)

Lawrence L. Garner.

Drozowska, S., Slomska, J., and Bega, J. **Titer of antistreptolysin in uveitis**. *Klinika Oczna* 26:193-198, 1956.

The authors review shortly the methods of diagnosing focal infection in uveitis. They measured the antistreptolysin levels in the serum and found it useful. The titer of streptolysin in the serum was higher in a number of cases of uveitis. In 14 of 16 cases in which the titer was high, antirheumatic treatment was successful. It was also successful in some of the cases with low titers. The authors feel that in uveitis of unknown etiology where the antistreptolysin level is high and where there is a positive uroprecipitation test, a rheumatic origin can be suspected. (2 tables, 14 references)

Sylvan Brandon.

Ikui, H. and Hiyama, H. **Clinical and experimental studies on idiopathic uveitis. Part II**. *Acta Soc. Ophth. Japan* 60:1687-1695, Nov., 1956.

The eye was removed for secondary glaucoma one year after the onset of the uveitis in a patient with Harada's syndrome. The authors found no histologic difference between Harada's syndrome and sympathetic ophthalmia. (7 figures, 7 references)

Yukihiko Mitsui.

9

GLAUCOMA AND OCULAR TENSION

Arriaga, Jose. **Traumatic glaucoma.** Arch. Soc. oftal. hispano-am. 16:666-670, July, 1956.

A case of traumatic glaucoma is reported, and its pathogenesis discussed. After an ocular contusion the patient developed traumatic iridocyclitis with hypertension. When the ocular tension continued to rise in spite of antihypertensive medication, cyclodiathermy and cyclodialysis were performed and the tension was controlled. The author points out that it is necessary to differentiate between a glaucoma secondary to a mechanical obstruction, as in dislocation of the lens or hyphema, and that caused by a disturbance in the vasomotor regulating mechanism of the uvea. He considers the latter as true traumatic glaucoma, while the former are hypertensions secondary to trauma. (1 figure, 4 references)

Ray K. Daily.

Arruga, H. **Diamox and glaucoma.** Arch. Soc. oftal. hispano-am. 16:627-631, July, 1956.

This is an addition to a report presented by Arruga at the French Ophthalmological Society in May, 1956, and to an article published in this journal in April, 1956. The present conclusions are based on experience in over 100 cases. The drug was effective in two thirds of the cases in which it was used, principally in acute glaucoma, in acute exacerbations of secondary glaucoma, in early cases of chronic inflammatory, in some cases of chronic simple glaucoma and in delayed reformation of the anterior chamber following cataract extraction, keratoplasty and fistulating operations. It is useful when a reduction of ocular tension is desirable, for intraocular operations, postoperative rises of ocular tension, and mydriasis in eyes with high ocular tension. Its toxicity

varies in different people; used with caution it may be tried in every case. Its prolonged ingestion is justifiable in patients in whom it is well tolerated and in whom the surgical risk is great. Ray K. Daily.

Auricchio, G. **The mechanism of action of cyclodialysis.** Boll. d'ocul. 35:401-411, June, 1956.

Having studied several cases of persistent ocular hypotonia following cyclodialysis, the author analyzes the hydrodynamic peculiarities caused by this operation. He emphasizes the differences between results after cyclodialysis and after other antiglaucoma operations. (2 figures, 16 references) William C. Caccamise.

Cortes de los Reyes, H. and Diaz Martinez, M. **New experiences with Diamox.** Arch. Soc. oftal. hispano-am. 16:632-639, July, 1956.

The literature is reviewed, and 15 cases are reported which illustrate the immediate effect of Diamox on the ocular tension. (6 references) Ray K. Daily.

Delmarcelle, Y. **Familial congenital glaucoma in two successive generations.** Bull. Soc. belge d'opht. 113:399-412, June, 1956.

Congenital glaucoma is believed to be transmitted as an autosomic recessive trait. In about 7 percent of the cases a known consanguinity exists; the parents of buphthalmic children are phenotypically healthy. The author observed two families with congenital glaucoma. The father and one child were affected in the first family and the father, a sister of the father and a child in a second family. To re-evaluate the hereditary trends, 21 cases of congenital glaucoma in successive generations were reviewed. The material was too small to allow an exact definition concerning the type of transmission. Nevertheless, this study is not only interesting but also of practical importance.

In general, children of parents with congenital glaucoma are believed to be spared by this disease. This opinion, however, should be expressed with certain reservations. (2 figures, 2 tables, 62 references)

Alice R. Deutsch.

Fritz, A. **Clinical ocular plethysmography.** Bull. Soc. belge d'opht. 113:412-423, June, 1956.

Clinical tonography registers the ocular tension before, during and after a predetermined application of an electronic tonometer; the tonographic curves however have shown considerable variation caused not only by differences in the technique but also by an inconsistency in the intra-ocular blood volume and by a changing tonus of the vascular walls and the rapid movement of the blood. Dynamometric compression of the eye raises the ocular tension in variable degrees even if this compression is lower than the intra-ocular blood pressure. If this progressive compression reaches a critical level, the space devoid of blood yields to the intra-ocular fluid and the further increase of ocular tension is stopped. The increase in ocular tension during this period is expressed by an equation $P = P_{02} - P_{01}$. The elevation in tension varies not only in normal and hypertensive eyes but also in the same eye during successive periods of registration. The relationship between the ocular tension and dynamometric compression deserves recognition and adequate interpretation during tonography. (5 figures, 8 references)

Alice R. Deutsch.

Hirokawa, T. **Gonioscopic studies of the anterior chamber. III-IV.** Acta Soc. Ophth. Japan 60:1718-1722, 1821-1825, Nov., Dec., 1956.

In miotic eyes the chamber angle is apt to be narrow and the converse is true in mydriatic eyes. In normal subjects there is no relation between the intra-ocular

pressure and the amplitude of the angle, color of the ciliary body band, pigmentation and brilliancy of the corneoscleral trabeculae, pigmentation of the Schwalbe's line and iris processes. Glaucoma may not be explained by the mechanical theory only. (10 tables, 25 references)

Yukihiko Mitsui.

Klemens, F. **Why total iridectomy?** Klin. Monatsbl. f. Augenh. 130:7-11, 1957.

A peripheral iridectomy was done in 32 patients with acute glaucoma; 29 of them remained cured. The author believes that peripheral and not total iridectomy should be the operation of choice. (8 references)

Frederick C. Blodi.

Nakaji, H. **Effect of convulsive shocks on ocular tension.** Acta Soc. Ophth. Japan 60:1808-1813, Dec. 1956.

Immediately after an electro- or cardiazole shock, there is an increase in the ocular tension in rabbits which lasts for the period of after-shock miosis (one-half to two minutes). The increase is then gradually followed by a negative phase in five minutes with an appearance of mydriasis, finally to recover the original tension in a course of one-half to one hour. The duration of the negative phase is apt to be longer after cardiazole than after electro-shock. The change in the systemic blood pressure is not parallel with that of the ocular tension. An administration of atropine, eserine (topical) or curare (systemic) does not seem to have any influence on the change in the ocular tension of shock (4 figures, 1 table, 14 references)

Yukihiko Mitsui.

Ohashi, K. **A new form of angiodiathermy in glaucoma with animal experiments.** A.M.A. Arch. Ophth. 57:41-48, Jan., 1957.

The author makes a series of diathermic perforating multiple coagulations along the long posterior ciliary artery tempo-

rally, going through an opening in the tendon of the lateral rectus muscle. He has used it favorably in all types of glaucoma, with the best results in simple glaucoma. Old glaucoma cases of angle-closure type need a combination with other procedures. Suppression of aqueous production is presumed to be the factor causing the favorable effect. (4 figures, 6 tables, 29 references) G. S. Tyner.

Taliercio, A. and Gemolotto, G. **A combined antiglaucoma operation.** *Boll. d'ocul.* 35:471-478, July, 1956.

The authors review the literature concerning combined antiglaucoma operations and describe their own technique in which they combine cyclodialysis with iridectomy and iridencleisis. In 33 cases of chronic simple glaucoma in which the combined operative procedure was employed, satisfactory results were obtained in 30. The operative technique is well illustrated. (4 figures, 15 references)

William C. Caccamise.

Valente, Adolpho. **Problems in the medical treatment of glaucoma.** *Arq. brasil. de oftal.* 19:6-52, 1956.

The etiology of primary glaucoma is uncertain, although both the mechanical and neurovascular theories have many supporters. Medical therapy discussed in this article concerns the latter theory. Our knowledge of neurophysiology and biochemistry suggests that there is a dynamic arteriocardillary mechanism regulating blood content, as well as a biochemical state of the capillary endothelium which depends upon neurovegetative equilibrium. Both of these mechanisms influence capillary permeability. Glaucoma is considered to have the aspect of a thalamic syndrome, since the ocular neurovascular mechanism is controlled by normal and pathologic daily stimuli. Glaucoma, therefore, should be classified as a thalamic hypersensitivity in which a

functional disturbance is characterized by diencephalic disorganization. Medical therapy is directed toward regulating arteriocardillary function and combatting the general causes which may disturb this function.

The author has treated 44 patients with various types of primary glaucoma, using such drugs combined with miotics when indicated. The greatest number (41) had chronic simple glaucoma. The results have been encouraging, with good or considerable improvement in most instances. It is believed that the therapy of glaucoma will be more medical and less surgical in time to come. (4 tables, 59 references)

James W. Brennan.

Weekers, R. Gougard, C., Gougard, L. and Watillon, M. **Ligation of the anterior ciliary arteries and diathermy coagulation at the entrance of the posterior ciliary arteries in the treatment of ocular hypertension.** *Bull. Soc. belge d'opht.* 113:423-431, June, 1956.

The ligation of all anterior ciliary arteries combined with a posterior cyclo-diathermy arrests the formation of the aqueous almost completely and causes severe degenerative changes in the iris, the lens and the nutritive mechanism of the inner eye. Whenever the secretion of the aqueous diminishes to less than 1mm.³/1min. an opacification of the lens is to be expected. The operation described in this paper deprives the ciliary body of a part of its blood supply, modifies the circulation of the whole uvea and decreases the production of aqueous in one minute to about 1mm.³ The technique is described as follows. After exposure of the internal rectus muscle, it is ligated with fine silk threads through the upper and lower half at the scleral insertion and about 3mm. behind the insertion. Five to six nonperforating diathermy punctures are made with a 2mm. thermometric electrode at 80°C for 15 seconds in the path of the

long posterior ciliary artery, in front of or just behind the insertion of the muscle. A similar procedure is done at the site of the external rectus muscle. The results of this operation in 14 patients are summarized. The indications for this operation and others for reducing the formation of aqueous, are discussed. (2 figures, 1 table, 16 references) Alice R. Deutsch.

Weekers, R. and Watillon, M. **A type of congenital glaucoma without megalocornea, and delayed incidence of hypertension.** Bull. Soc. belge d'opht. 113:308-316, June, 1956.

There are three forms of congenital glaucoma. The classical form which does not need any comment, the megalocornea which is visible at birth but only occasionally precedes an increase of ocular tension in later life, and the so-called congenital glaucoma without megalocornea or enlargement of the globe. This last kind of glaucoma is the subject of this paper. It is a rare disease. The hypertension manifests itself between the first and third decade. A characteristic greenish, felt-like tissue, covering the ciliary band is visible on gonioscopic examination. Occasionally some abnormal vessels are visible. The trabecular band is visible, at least partly, and always very pigmented, whereas this is not true in classical congenital glaucoma. Corneal marginal dystrophy of moderate degree was seen in some cases. Whenever tonography was done the resistance to the outflow of aqueous was found to be increased. The late occurrence of the hypertension was ascribed to a migration of pigment towards a partially closed chamber angle, accumulation of pigment in the trabeculae and premature sclerosis of the emissary channels. Miotics are ineffective as in other forms of congenital glaucoma and drugs which reduce the formation of the aqueous are not advantageous in extended use. Iridencleisis is the surgery of choice and

has been successful in the authors' hands. Goniotomy and cyclodiathermy are not advised. Four case histories are reviewed. (4 figures, 8 references)

Alice R. Deutsch.

10

CRYSTALLINE LENS

Appelmans, M., Michiels, J. and François, J. **Cataract in myotonia.** Bull. Soc. belge d'opt. 113:372-380, June 1956.

The histories of two patients with myotonic cataract are reported. Both patients presented the characteristic muscle changes, the cataracts and divers endocrine abnormalities transmitted through three generations. The normal calcium and phosphorus values in the blood, the typical myographic curves and the presence of iridescent cortical lens opacities were considered to be of differential-diagnostic significance. In both patients the cataracts had to be extracted extracapsularly because the zonula was difficult to strip and because the capsules were stretched and could not be grasped with an Arruga forceps. The cause of this rare disease may be a disturbance in the protein metabolism. The breakdown of glycogen under anaerobic conditions furnishes the basic requirement for muscle contraction. Other substances indispensable to the metabolism of the muscle are adenyolphosphoric acid, creatine-phosphoric acid and phosphorolytic enzymes. An irregularity in the process probably is the origin of the abnormality in muscular structure and function and the present clouding of the lens. (6 figures, 11 references) Alice R. Deutsch.

Bozzoni, F. **Cataract extraction with the assistance of expressors which can be manipulated with one hand.** Boll. d'ocul. 35:380-383, May, 1956.

The author describes a type of finger expressor which can be used during cata-

ract surgery. One ring-like expressor is attached to the thumb and another one is attached to the index finger. With these expressors the surgeon is able to exert pressure and counter-pressure with one hand. The author feels that this is of assistance when the surgeon is operating without a qualified assistant. (3 figures)

William C. Caccamise.

Bryk, Edward. **Generalized argyrosis with involvement of lenses.** *Klinika Oczna* 26:217-219, 1956.

A man, 76 years of age, showed signs of generalized argyrosis with silver deposits in the lenses. Before the operation the lenses were bluish-gray and shiny. The lenses were removed in the capsule and examined microscopically. Silver deposits were scattered through all the layers but the greatest accumulation was in the capsule. The function of the eye was very little affected by the argyrosis. Vision with correction was 6/6. (3 figures, 2 references)

Sylvan Brandon.

Chavarria Iriarte, R. **Congenital subluxation of the lenses.** *Arch. Soc. oftal. hispano-am.* 16:678-683, July, 1956.

The author reports a case of congenital subluxation of the lenses, in a woman, 37 years old, without other symptoms of Marfan's syndrome. The family history revealed a large number of members with a similar disturbance. There was also a history of family consanguinity. The patient later developed retinal detachment in both eyes and cataract in the right eye. The right eye was operated upon for retinal detachment, and subsequently, when the cataract was dislocated into the vitreous, it was extracted; the result was a total loss of vision. Some vision remained in the left eye, which had not been operated upon because of the poor surgical result in the right eye. (4 references)

Ray K. Daily.

Hilding, A. **Pupillary blockage by a subluxated lens, causing glaucoma.** *A.M.A. Arch. Ophth.* 57:33-36, Jan., 1957.

The arguments for and against surgery in dislocated lenses in children is discussed. A bilateral case with glaucoma and the surgical cure are reported. (3 figures, 8 references)

G. S. Tyner.

Rumbaur, W. **Extraction of a lens luxated into the vitreous.** *Klin. Monatsbl. f. Augenh.* 130:12-17, 1957.

The author re-emphasizes his method originally described in 1946. The lens is visualized with a transilluminator held against the sclera. A diathermy needle, introduced near the limbus, is anchored to the lens and pushes it into the pupil. It is held there while the extraction with loop or forceps follows. Loss of vitreous can usually be avoided. (1 reference)

Frederick C. Blodi.

11

RETINA AND VITREOUS

Auricchio, G. **The pathology of the detached retina: the alkaline reserve of the subretinal fluid.** *Boll. d'ocul.* 35:337-344, May, 1956.

Under normal circumstances the vitreous has a higher bicarbonate ion content than the plasma. However, interference with the blood circulation causes a reduction in the ratio of intraocular bicarbonate ion to blood bicarbonate ion. In contrast to the vitreous, the subretinal fluid in cases of retinal detachment contains less bicarbonate ion than the blood plasma. The separation of the retina from the choroidal vasculature causes an intraocular acidosis. (2 figures, 5 references)

William C. Caccamise.

Colyear, B. H., Jr. and Pischel, D. K. **Clinical tears in the retina without detachment.** *Tr. Pacific Coast Oto-Ophth. Soc.* pp. 185-219, 1955.

Cases of retinal tear without detachment and others with it are evaluated in an attempt to establish a means of prognosis. Although detachment did not occur in 40 percent of the cases in which a hole was found, prophylactic operation should probably be done. Nonpenetrating diathermy at this stage is a relatively simple procedure, and partially penetrating needles with low milliamperage readings of 20 to 30 are recommended. (75 references)

Lawrence L. Garner.

Coppez, L. and Szucs, S. **Statistical review of detachment operations.** Bull. Soc. belge d'ophth. 113:672-94, June, 1956.

During 1949 to 1954, 243 detachments were operated upon. The diathermy coagulation with the pyrometric electrode introduced and perfected by L. Coppez, was the method of choice. Recovery was complete in 54.7 percent, anatomic recovery was seen in 22.4 percent, and failure in 22.8 percent. The predisposition of myopic eyes to detachment was confirmed. There was no association of place and type of tear with refraction. Multiple tears were mostly found in myopes. The prevailing location of tears in the superior temporal quadrant was tentatively ascribed to the traction of the superior oblique muscle or to some vascular deviation in this sector. A detachment older than six months and extending over several quadrants was always considered unfavorable. The age of the patient also is important. Between the ages of 61 and 70 years the recovery rate was 47.7 percent; between 71 and 80 years only 20 percent. Bilateral detachments showed an unusually good recovery, in this series 66 percent. Of traumatic detachments 42.5 percent were cured. Retinal disinsertion showed no characteristic location and did not favor myopes but definitely impaired the hope for cure. The same was true for detachment of the macula. Coincident ocular hypertension was an unfavorable

factor; only two cures were accomplished in nine cases. A co-existing chorioretinitis did not affect the outcome in traumatic detachments. (8 figures, 9 tables, 2 graphs, 37 references)

Alice R. Deutsch.

Ferreira, L. E. **Recurring juvenile hemorrhages in the vitreous.** Rev. brasil. oftal. 15:379-398, Dec., 1956.

The author gives a fairly complete historical summary of the literature and discusses the various theories of origin such as tuberculous periphlebitis, thromboangiitis obliterans, blood dyscrasia, infection and endocrine disturbance. This disease may be manifest in macular hemorrhages, retinal hemorrhages extending into the vitreous and retinitis proliferans. The author outlines some of the forms of treatment which have been advocated. He presents three cases of hemorrhage in the vitreous. In the first one hemorrhage was due to periphlebitis, and was followed by retinal detachment in one eye, one was traumatic and in the other case a hemorrhage in the macular area cleared after a tonsillectomy. (2 figures, 13 references)

Walter Mayer.

François, J. and Verriest, G. **Detection of acquired dyschromatopsias in tapeto-retinal degenerations with the tests of Farnsworth.** Bull. Soc. belge d'opht. 113:381-398, June, 1956.

The tests of Farnsworth represent a valuable assistance for the fundamental investigations of dyschromatopsias and allow the classification of acquired dyschromatopsias except during either a very early stage or the terminal stage of these diseases. The test consists of three parts. Panel D-15 permits an immediate differential diagnosis of mild anomalies by accentuation of the axes of confusion. The Farnsworth Munseel 100 hue test for color discrimination outlines the axis of dyschromatopsia even more precisely and allows the detection of supra- and infra-

normal differential color perception. The polychromatic plates of Farnsworth (Tritan plates) make the diagnosis of congenital Tritanomalies possible, as well as recognition of protonanomalopsias and deuteranomalopsia.

Fourteen cases of chorioretinal degeneration were thoroughly studied. Among them were 11 cases of retinopathia pigmentosa, one of retinopathia punctata albescens, two of anterior chorioretinal abiotrophy and two of juvenile macular degeneration. A dyschromatopsia with affection of the blue-yellow sensation was found in the patient with peripheral chorioretinal degeneration. There was a variation of the axis from the deuteranopic to the tetraanopic axis with a maximum of frequency in the proximity of the tritanopic axis. A dyschromatopsia especially toward the red-green sensation was found in the patients affected with Stargardt's degeneration of the macula. In one case of juvenile degeneration of the macula complete central loss of color perception was found. In a monocular case of retinopathy pigmentosa the vision of the diseased eye was too poor to be tested but the other eye had normal color perception, a further argument for the possible monocular existence of this disease. (10 figures, 6 references)

Alice R. Deutsch.

Frohmann, Clemens. **A case of unilateral retinitis pigmentosa.** *Klin. Monatsbl. f. Augenh.* 130:102-105, 1957.

In a 27-year-old woman who could be followed for two years the left eye showed all the characteristics of retinitis pigmentosa, including dark adaptation and electroretinogram, while the right eye remained entirely normal. (2 figures, 4 references)

Frederick C. Blodi.

Marin-Amat, M. **Present status of treatment of retinal detachment. Improved prognosis.** *Arch. Soc. oftal. hispano-am.* 16:652-662, July, 1956.

The author advocates extensive diathermy coagulation with drainage of the subretinal fluid in preference to scleral resection. Six cases are reported to illustrate the effectiveness of the author's procedure. In early cases with limited detachment, superficial coagulation with one or two drainage punctures suffices to reattach the retina. In old and extensive detachments the coagulation should extend over the entire area of detachment and the subretinal fluid should be evacuated completely. The author considers this procedure simpler and more effective than a scleral reaction. (11 references)

Ray K. Daily.

Melanowski Wladyslaw, H. and Kobszewska-Faryna, M. **Retrolental fibroplasia and hydrophthalmia.** *Klinika Oczna* 26:199-205, 1956.

In two cases of retrolental fibroplasia the eyes were operated upon for increased intraocular pressure, nevertheless hydrophthalmia developed and eventually the eyes had to be enucleated. The authors feel that hydrophthalmia was not caused by retrolental fibroplasia but by the primary disease of the capillary vessels. There was evidence of underdevelopment of Schlemm's canal and of the angle of the anterior chamber. Retrolental fibroplasia and angiomas appear later. (9 figures, 8 references)

Sylvan Brandon.

Rome, Sol. **Heparin in senile macular degeneration.** *A.M.A. Arch. Ophth.* 57:190-199, Feb., 1957.

Because of its lipemia-clearing action, heparin is now being used as an antiatherogenic agent and it was postulated that it might have some affect in senile macular degeneration. In March, 1952, a study was begun on 23 such patients who had had other types of therapy. Dosage arbitrarily used in this study was 100 mg. of the sodium salt of concentrated aqueous heparin given intravenously twice weekly.

A series of 10 to 20 injections was given, followed by a two to three week interval. There was moderate to marked improvement in more than half of the patients. The only contraindications to heparin therapy are active internal ulceration, chronic liver disease, and a hemorrhagic diathesis. No untoward reactions were noted in more than 1,000 intravenous injections. (3 figures, 2 tables, 29 references)
G. S. Tyner.

Stark, Hilmar. **The effect of heparin on retinal arterial occlusions caused by atherosclerosis.** Klin. Monatsbl. f. Augenh. 130:72-82, 1957.

Nine patients with acute occlusion of the central retinal artery were treated with anticoagulants. The results were promising. (21 references)

Frederick C. Blodi.

Vigorelli, E. and Zanotti, G. **Hypertensive retinopathy and cochlear function.** Riv. oto-neuro-oftal. 31:519-529, Nov.-Dec., 1956.

Thirty patients with hypertensive retinopathy, Keith-Wagener stages 3 and 4, were studied from an acoustic point of view. The authors attempted to correlate the hypertension with cochlear function and retinal vascular manifestations with acoustic function. Their studies revealed that the labyrinthine structures may be affected by the hypertension, but that the relationship is not a constant one. There also seemed to be a certain parallelism between acoustic function and the degree of retinal vascular change. (3 tables, 9 references)
William C. Caccamise.

Volckmar, Hans. **Subconjunctival implantation of placenta in degenerative lesions of the fundus.** Klin. Monatsbl. f. Augenh. 130:82-86, 1957.

Of 10 patients with retinitis pigmentosa six got worse and four remained unchanged. Among 36 eyes with high

myopia nine had a slight improvement, nine a slight deterioration and in 15 eyes no change was noted. Among five patients with senile macular degeneration no long-lasting improvement could be obtained. (3 tables)
Frederick C. Blodi.

Wolter, J. Reimer. **Development and nature of drusen of the retinal pigment epithelium.** Klin. Monatsbl. f. Augenh. 130:86-95, 1957.

These drusen may occur as hyaline transformation of pigment epithelial cells or as deposition of hyaline on Bruch's membrane. Both possibilities were found in flat and cross sections of a human eye stained with silver carbonate. (8 figures, 19 references)
Frederick C. Blodi.

12

OPTIC NERVE AND CHIASM

Helmick, Ernest D. **Tabetic optic atrophy.** A.M.A. Arch. Ophth. 57:282-285, Feb., 1957.

The author reports a case of tabetic optic atrophy observed over a 15-year period without change, in which, peculiarly, only 1,200,000 units of penicillin were used. (2 figures, 1 reference)

G. S. Tyner.

Keefe, R. and Trowbridge, D. **Neuro-myelitis optica with increased intracranial pressure.** A.M.A. Arch. Ophth. 57:110-111, Jan., 1957.

A 13-year-old girl had sudden bilateral blindness, marked papilledema, and very high increased intracranial pressure. She recovered, but with bilateral optic atrophy and very poor vision.
G. S. Tyner.

Ricci, A. **A case of unilateral subacute edematous optic neuritis.** Riv.-oto-neuro-oftal. 31:530-538, Nov.-Dec., 1956.

The author emphasizes the difficulty that may be encountered in differentiating optic neuritis from choked disc. This is particularly true in optic neuritis with

normal visual acuity. It is in such cases that field studies are of the utmost importance in the differential diagnosis. The author describes in detail the case of a 40-year-old farmer with 20/20 vision in both eyes but papilledema in the left eye. Perimetric studies revealed definite peripheral constriction in the left eye which lead to a diagnosis of optic neuritis instead of choked disc. (5 figures, 4 references)

William C. Caccamise.

Trzcinska-Dabrowska, Zofia. **Glioma of the optic nerve.** *Klinika Oczna* 26:207-211, 1956.

The author presents two cases of glioma of the optic nerve, one in an 18-year-old girl who had exophthalmus for three years and the second in a three-year-old girl in whom symptoms appeared three months before the examination. Tumors were removed by orbitotomy according to Krönlein and cutting the nerve near the apex of the orbit, leaving the globe intact. Microscopic examination showed that there was no intracranial extension of the glioma and that both were spongioblastoma polare. Observation for more than a year did not disclose any recurrence. (7 figures)

Sylvan Brandon.

13

NEURO-OPHTHALMOLOGY

Alexander, H. **Vascular lesions affecting the visual pathways.** *A.M.A. Arch. Ophth.* 57:65-75, Jan., 1957.

This essay deals primarily with disturbance of the visual pathways by lesions in the temporal isthmus and in the occipital lobes. Excellent case reports and photographs of sections of the brain form the basis of the discussion. (8 figures, 7 references)

G. S. Tyner.

D'Ermo, F. **A rare ocular complication of multiple sclerosis.** *Boll. d'ocul.* 35:436-444, June, 1956.

The author reviews the literature on periphlebitis retinae and the inflammatory processes of the uveal tract that have been reported in cases of multiple sclerosis. Such ocular complications occur very rarely in this disease. The author then discusses the case of a 50-year-old woman with multiple sclerosis who had bilateral iridocyclitis and secondary glaucoma in one eye. Laboratory studies were completely negative and the author suggests that the uveitis can be attributed to an allergic reaction in the uvea to the virus that is the cause of the multiple sclerosis. (23 references)

William C. Caccamise.

Elander, C., Bedrossian, R. and Schaerer, J. **Unilateral lid retraction.** *A.M.A. Arch. Ophth.* 57:37-38, Jan., 1957.

The syndrome of unilateral lid retraction is discussed, and a case associated with spontaneous thrombosis of the common carotid artery is presented. (2 figures, 4 references)

G. S. Tyner.

Galvez Montes, J. **Quantitative nystagmography. Amplitude and frequency of ocular movements.** *Arch. Soc. oftal. hispano-am.* 16:742-749, Aug., 1956.

Using an instrument similar to a cardiograph, the author analyzed excursions amplitudes and frequency in ten subjects. The conclusion emerging from this study is that the registered voltage is directly proportional to the amplitude of the movements, and inversely proportional to the square of the time. (2 graphs, 2 tables)

Ray K. Daily.

Magistretti, A. **Parinaud's syndrome in neuromuscular diseases.** *Boll. d'ocul.* 35:352-363, May, 1956.

The author discusses the case of a 32-year-old man with myasthenia gravis and a 36-year-old man with dystrophia myotonica (Steinert's disease). Both patients had a marked impairment of voluntary elevation of the eyes with, however,

a retention of Bell's phenomenon. (28 references) William C. Caccamise.

Sonntag, Richard W. **Optochiasmic arachnoiditis.** Tr. Pacific Coast Otol. Soc. pp. 143-157, 1955.

The literature is briefly reviewed and the diagnostic problems are discussed. Headache is one of the earliest symptoms and is followed by visual loss. The latter may be slow or rapid and may occur in one or both eyes. Visual field changes are very variable but important in the diagnosis. The fundus may be normal or show evidences of optic nerve changes. Surgery should be urged early since it is then that best results are obtained. It has been shown that 35 percent of all patients who have been operated upon show some improvement of visual acuity, although loss of vision is usually severe by the time the diagnosis is made. (10 figures, 7 references) Lawrence L. Garner.

14

EYEBALL, ORBIT, SINUSES

Finkemeyer, H. and Heck, E. **Etiology and pathogenesis of a pulsating exophthalmus.** Klin. Monatsbl. f. Augenh. 130: 63-71, 1957.

A unilateral exophthalmus developed in a 40-year-old man after a gunshot injury to the head. Angiography on that side revealed an occluded internal carotid artery and a large saccular aneurysm over the external carotid which communicated with the ipsilateral vertebral artery. The jugular vein was occluded toward the vena cava and that forced the arterial blood into the cranium producing the exophthalmus. (5 figures, 8 references) Frederick C. Blodi.

15

EYELIDS, LACRIMAL APPARATUS

Beard, C. **Lids, lacrimal apparatus, and conjunctiva.** A.M.A. Arch. Ophth. 57:112-133, Jan., 1957.

This excellent review is made even more valuable by the reviewer's pertinent remarks based on his wide experience. (135 references) G. S. Tyner.

Gandolli, A. **A new type of plastic surgery of the upper lid.** Boll. d'ocul. 35: 364-371, May, 1956.

The author describes a new type of plastic operation which he used in treating a patient with a diffuse carcinoma involving the entire upper lid. The upper lid is reconstructed by means of a pedicle skin flap taken from the frontal region. Buccal mucosa is used as a conjunctival substitute. The entire procedure is depicted in detail. (8 figures)

William C. Caccamise.

Janiszewska Gelder, Barbara. **Actinomycosis of the lid and soft parts of the skull.** Klinika Oczna 26:221-225, 1956.

The author presents a case of actinomycosis of the lids of the left eye and of the soft tissues over the left side of the head in a boy, 14 years of age. The disease was present for three months when diagnosed. When first seen sarcoma was suspected but actinomycosis was diagnosed on the bases of eosinophilia, normal appearance of bone, draining fistulae and microscopic examination of secretion. Treatment consisted mainly of systemic and local application of penicillin and lasted 16 weeks; 30 million units of penicillin were used. Only slight scarring remained visible at the time of discharge from treatment. (4 figures, 6 references)

Sylvan Brandon.

Le Grand, P. **Reevaluation of the lacrimal duct-intubation one year after the operation.** Bull. Soc. belge d'opht. 113: 431-436, June, 1956.

The intubation of the lacrimal duct and application of a filiform drainage for 15 days, as described previously by Dejean, was performed on ten patients with epiphora and 15 with dacryocystitis. The favor-

able cases were 68 percent of the series at the end of two months, but only 52 percent after one year. Bietti had found 80 percent failure after three years. A granulomatous, hypertrophic dacryocystitis with destruction of the epithelium and lymphomatous and plasma-cell infiltration in the walls was found by François in a lacrimal sac which, initially successful, had to be removed after an intubation. Intubation should only be used rarely and only in very old or debilitated persons in whom a dacryocystorhinostomy is not advisable. (13 references)

Alice R. Deutsch.

Mackensen, G. **The treatment of dacryocystitis in infants.** Klin. Monatsbl. f. Augenh. 130:17-25, 1957.

The probing is done with a Bowman probe which is curved at the end. The probe is turned at the nasal end of the duct so that the tip points toward the nasal cavity. This allows a wide opening of the occluding membrane. Out of nine infants with protracted dacryocystitis seven could be cured with this type of probing. The other two had to be operated on. (13 figures, 3 references)

Frederick C. Blodi.

Marin Amat, M. **An operation for partial entropion.** Arch. Soc. oftal. hispano-am. 16:722-727, Aug., 1956.

The author considers the operation described by Larmande inadequate and temporary in its effect. The author's procedure consists of 1. an incision through the skin and orbicularis 2 or 3 mm. from the lashes, 2. excision of the hypertrophied orbicularis fibers in the incision, 3. section of the cartilage as close to the lashes as possible, 4. thinning of the cartilage and 5. sewing the lower portion of the cartilage to the upper thinned portion with Panas' sutures, in such a manner that the lashes turn outwards. (11 figures)

Ray K. Daily.

Mielnick, I. and Przyborowska, H. **Management of congenital ankyloblepharon internum.** Klinika Oczna 26:249-251, 1956.

Ankyloblepharon internum in a 19-year-old boy is described. The palpebral fissure was only 24 mm. long; the lacrimal canaliculi were present and were of double length. The skin was cut between the canaliculi and sutured as in canthotomy. (3 figures, 1 reference) Sylvan Brandon.

Milam, D. **Mikulicz's disease of the lacrimal gland.** A.M.A. Arch. Ophth. 57:236-240, Feb., 1957.

Four cases from the Massachusetts Eye and Ear Infirmary are reported. The disease is characterized by epimyoeptithelial islands, intraduct proliferation of epithelial and myoeptithelial cells, and sheets of lymphoid cells. (5 figures, 5 references)

G. S. Tyner.

Phillips, C. I. and George, M. **Epiphora and the bony naso-lacrimal canal.** Brit. J. Ophth. 40:673-680, Nov., 1956.

By the use of a dental X-ray film held in the mouth, it is possible to obtain a radiographic view of the opening of the nasolacrimal canal "end-on" and the opening of the canal can be measured. Seventeen patients complaining of epiphora for which no external cause could be found were thus studied and compared with 12 controls. The studies revealed no appreciable difference between the patients and the controls or between the two sides in the unilateral cases. Although bony abnormalities may sometimes account for epiphora, their importance as a cause of epiphora must be small. (3 figures, 2 tables, 14 references) Morris Kaplan.

Soares, R. **Bilateral coloboma of the upper lids.** Rev. brasil. oftal. 15:451-460, Dec., 1956.

The author gives a brief summary of the literature on colobomata of the lids and the associated congenital anomalies in the eyes and also in other systems. He

briefly reviews the various theories of their origin and presents a case in which he plans to operate in two stages: a blepharoplasty followed by a lamellar keratoplasty to free the cornea from its covering cutaneous band. (2 figures, 9 references) Walter Mayer.

Velhagen, Karl. **The lagophthalmus operation of Lexer-Rosenthal.** Klin. Monatsbl. f. Augenh. 130:1-7, 1957.

This operation consists of a transplantation of a part of the temporalis muscle into the upper and the lower lid. Five patients were operated on and in three of them the result was quite satisfactory. (16 figures, 3 references)

Frederick C. Blodi.

16

TUMORS

Cogan, John F. **Extramedullary plasmocytoma of the orbit.** Brit. J. Ophth. 40: 681-685, Nov., 1956.

Plasmocytomata are tumors of plasma cells which may be primary anywhere in the body. They may be single or multiple, benign or malignant tumors and must be followed for years before a final prognosis can be given. Two cases of plasmocytoma of the orbit and of the lacrimal sac are described. One was a single, isolated, benign tumor and the other was malignant and was followed several years later by a similar tumor in the colon. In neither case was the eye itself involved. (2 figures, 19 references)

Morris Kaplan.

Damato, F. J. and Damato, T. J. **Orbithmoidal osteoma.** A.M.A. Arch. Ophth. 57:290-294, Feb., 1957.

A case of unilateral proptosis and papilledema in a 13-year-old girl is reported. (4 figures, 9 references) G. S. Tyner.

Das Gupta, B. K., Sen, G. C. and Basu, R. K. **Lymphocytoma of the orbit.** Brit. J. Ophth. 40:669-672, Nov., 1956.

Lymphomatous tumors are not infrequently found in the orbit although normally there is no lymphoid tissue there. There are three types: lymphocytic cell type, reticulum cell type and giant follicular type. A 42-year-old man complained of fullness of the right upper and lower lids and gradual painless proptosis. A mass could be felt through the lids but the eye itself was normal. The encapsulated tumor was easily removed and healing was uneventful. The histologic diagnosis was lymphocytoma. (3 figures, 17 references) Morris Kaplan.

Del Duca, A. **A case of orbital reticulosarcoma.** Boll. d'ocul. 35:372-379, May, 1956.

The author describes the case of a 50-year-old woman with reticulosarcoma of the right orbit. The lesion had been present for at least six years. Diagnosis was established by means of biopsy. Apparently satisfactory results were obtained with chloronaftine and X-ray therapy. (6 figures, 47 references)

William C. Caccamise.

Dyson, C. **Chordomas of ocular interest.** A.M.A. Arch. Ophth. 57:19-23, Jan., 1957.

Malignant chordomas associated with eye signs are discussed and a case is reported. (4 figures, 23 references)

G. S. Tyner.

Krug, A. and de Barros, M. **Morphological and statistical study of lid tumors.** Rev. brasil. oftal. 15:411-418, Dec., 1956.

The authors present a tabulation of the ocular tumors they have examined in their laboratory during the past five years and propose a new classification in three groups: 1. epithelial, 2. conjunctival and 3. tumors whose origin is uncertain. Neoplasms in group 3 are considered epithelial by some authors and pigmented by others. In each of these groups tumors can be

benign or malignant and primary or metastatic. (3 tables, 6 references)

Walter Mayer.

Ostriker, Paul J. **Metastasis of adenocarcinoma of colon to conjunctival surface of lid.** A.M.A. Arch. Ophth. 57:279-281, Feb., 1957.

Primary lesions of the eyelids are common, but metastasis from a distant malignant tumor is rare. A case of adenocarcinoma of the colon with a metastasis on the conjunctival surface of the lid is reported. (1 figure, 6 references)

G. S. Tyner.

Trzcinska-Dabrowska, Zofia. **Hemangiopericytoma of the lid.** Klinika Oczna 26: 213-216, 1956.

The author presents a case of hemangiopericytoma of the lid in a woman, 28 years of age. A small tumor had been removed from the right lower lid in 1950. Microscopic examination suggested sarcoma. The area of the wound was irradiated with X rays. In 1955 the woman came back with a recurrence. Again a tumor of the size of a cherry was removed. More detailed microscopic examination suggested hemangiopericytoma. The area of the wound was again treated with X rays. The author feels that because of invasive characteristics of the tumor, recurrence may be anticipated and a more radical operation will be necessary. (2 figures, 1 reference)

Sylvan Brandon.

Vila-Coro, A. and Coret, A. **Macroscopic anatomy of sarcoma of the choroid.** Arch. Soc. oftal. hispano-am. 16:641-651, July, 1956.

The data of the macroscopic anatomy of 38 cases of sarcoma of the choroid are summarized. The outstanding findings of this investigation are: 1. diffuse forms of the tumor were found as frequently as circumscribed forms, which does not support Fuchs's statement that the diffuse form is rare, 2. Lagrange's contention that

the diffuse forms are usually metastatic carcinomas is also not supported by the analysis of this material, 3. Fuchs's statement that melanomas originate as nonpigmented tumors is also refuted; in this material leucosarcomas maintained their color from their origin to the end, and melanomas were strongly pigmented from the beginning. Among the 38 tumors, five were leucosarcomas. (12 figures)

Ray K. Daily.

17

INJURIES

Chavarria Iriarte, Felix-Angel. **Ocular changes produced by photoelectric trauma.** Arch. Soc. oftal. hispano-am. 16: 671-677, July, 1956.

The literature is reviewed, and a case reported. A worker was struck by a short circuit of 30,000 volts. The following day he noticed a disturbance of vision, photopsia, photophobia, conjunctivitis and palpebral edema. These lasted a day and a half but he was left with cloudy vision. Examination revealed slight opacification of the lenses, and some contraction of the visual fields. The condition improved under therapy with calcium iodide and vitamins. (1 figure, 4 references)

Ray K. Daily.

Gil del Rio, E. **Ocular manifestations of erysipelotheix rhusiopathiae.** Arch. Soc. oftal. hispano-am. 16:694-696, July, 1956.

This disease, common in pigs, may be communicated to man through abrasions of the skin. The author reports two cases. One of the patients was injured on the external portion of the lower lid and, after a period of symptomless incubation, developed a sensation of burning in the lids which was accentuated by heat and diminished by cold. Erythema of the entire lid was noted which progressed to an edema which involved the upper lid. The preauricular and cervical lymph glands were swollen and painful. The general symp-

toms were those of septicemia. The second patient was struck with a piece of pork bone in the conjunctiva and developed an inflammation of the eyeball with the same general symptoms as in the first case. The causative micro-organism was isolated from the secretion. Therapy consists of high doses of penicillin and specific serum. Both patients were well in four days.

Ray K. Daily.

Meřz, Marian. **Eye injuries.** Klinika Oczna 26:235-244, 1956.

The author analyzes 780 eye injuries seen in the Warsaw Eye Clinic during the five years from 1949 to 1953: 246 occurred in children. Treatment is described and the final results are presented. Nine statistical tables give all important data. Enucleations were performed in 132 cases or 16 percent. There were three cases of sympathetic ophthalmia. (1 figure, 9 tables, 27 references)

Sylvan Brandon.

Meyer, F. W. **Injury to the eye with a sliver of glass.** Klin. Monatsbl. f. Augenh. 130:59-63, 1957.

The effect of glass as an intraocular foreign body is usually a mechanical one. It is well tolerated in the lens and the vitreous. A young man was seen who had a small fragment of glass in his anterior chamber for nearly ten years. The eye was occasionally irritated. The foreign body had to be extracted with the patient sitting at the slitlamp. (11 references)

Frederick C. Blodi.

18

SYSTEMIC DISEASE AND PARASITES

Applemans, M., Lobas, P. and Missotten, L. **The manifestations of avitaminosis A.** Bull. Soc. belge d'opht. 113:327-358, June, 1956.

The functional pathology of avitaminosis A and hypo-avitaminosis A is very difficult to evaluate because an occurrence

of other vitamin-deficiencies, a depletion of essentials of nutrition and disturbances in the metabolism of various organs may either suggest or mask the characteristic clinical picture. There is no strict relationship between the amount of vitamin A found in the blood and abnormalities in dark adaptation. The normal vitamin A content of the blood equals 0.7-1.3 UI/cm.³ Normal dark adaptation was found with 0.6 UI/cm.³ and abnormal dark adaptation with 2.0 UI/cm.³ The chronology of the conjunctival-corneal lesions in xerophthalmia was listed as follows: pre-xerosis, conjunctival xerosis, corneal xerosis and keratomalacia. In infancy keratomalacia may appear quickly without previous conjunctival xerosis. Bitot spots are a late manifestation and only develop in adults. They are irreversible; the same is true for keratomalacia. Conjunctival xerosis is a sign of active vitamin A insufficiency and is reversible. However, essential xerosis is not always a symptom of vitamin A insufficiency and is not inevitably preceded by hemeralopia.

Vitamin A insufficiency and related disturbances as seen during the stay in India by one of the authors are described. Observations of a severe case of vitamin A insufficiency in a 51-year-old Belgian man are discussed in detail. A clinical review of the whole subject is also included. (8 figures, 29 references) Alice R. Deutsch.

Appelmans, M. and Michiels, J. **Ocular onchocerciasis in a European after a three-year stay in Africa.** Bull. Soc. belge d'opht. 113:494-500, June, 1956.

The ocular lesions in onchocerciasis are caused by the presence of the microfilaria which invade the ocular tissue insidiously with preference of the limbus or subconjunctiva. They can be visible in slitlamp examination. The inflammation often is very mild or may be a punctate keratitis with extreme photophobia, plastic iritis and nodular conjunctivitis. Optic atrophy

has been described but other lesions of the posterior segment are very rare. The record of a 51-year-old man is reviewed. He had spent 17 years in the Belgian Congo. He had a severe iritis of the right eye. In his left, noninflamed eye a larva of *Onchocerca volvulus* was visible. No increase of proteins or cells was found on puncture of the anterior chamber. The W.B.C. showed 13 percent eosinophiles. The biopsy of a trochanteric lymph node demonstrated a large number of nematodes surrounded by connective tissue and many nematode embryos. It is characteristic for the *Onchocerca* to avoid the bloodstream but to spread through connective tissue. (5 figures, 11 references)

Alice R. Deutsch.

Eickemeyer, K. A. **Internal ophthalmomyiasis.** Klin. Monatsbl. f. Augenh. 130:95-102, 1957.

The negative phototaxis of most larvae speaks against the theory that they always reach the eye via sclera and vitreous (Kiel). In the author's case the larva was in the vitreous and disappeared when exposed to the bright light of a camera. The eye was eventually lost. (2 figures, 1 table, 9 references)

Frederick C. Blodi.

François, Jules. **Ocular toxoplasmosis.** Schweiz. Arch. f. Neurol. and Psychiat. 78:87-137, 1956.

François reports 28 cases of congenital ocular toxoplasmosis and draws attention to the specificity of the chorioretinal lesions. The entire group is reported in detail with fundus drawings of each case. Significant data such as age, presence of nystagmus or strabismus, cranial calcification, and dye tests are given in a four page table at the end of the article. In 80 percent of the cases the lesion was macular, in 20 percent peripheral. In one case the parasite was seen on histologic examination of the eye. Eleven patients

had a dye-test titer of over 1/64, five showed a typical macular atrophic lesion, and in the remaining 11 cases the author feels that the diagnosis is probable but not certain. (31 figures, 3 tables, 5 references)

David Shoch.

Irvine, A. Ray, Jr. **Temporal arteritis.** Tr. Pacific Coast Oto-Ophth. Soc. pp. 137-142, 1955.

Two cases of temporal arteritis are reported in which a possible relationship to drug sensitivity is suggested. The first patient showed an early reaction to an intramuscular test dose of gold chloride, and the second a mild anaphylactic reaction after an injection of penicillin. (6 figures)

Lawrence L. Garner.

Palomar Palomar, Alejandro. **Ophthalmologic manifestations of diabetes mellitus.** Arch. Soc. oftal. hispano-am. 16:827-1067, Sept., 1956.

This is a comprehensive monograph, which does not lend itself to abstracting. (33 figures, 405 references)

Ray K. Daily.

19

CONGENITAL DEFORMITIES, HEREDITY

Bonaccolto, G. **Congenital coloboma associated with cystic degeneration of the ciliary body.** A. M. A. Arch. Ophth. 57:18, Jan., 1957.

The author reports a case of coloboma of the lens which is believed to have developed as a result of congenital cystic formations in the ciliary processes pressing upon the equator of the lens.

G. S. Tyner.

Rizzo, U. A. **Marfan's syndrome.** Rev. brasil. oftal. 15:401-409, Dec., 1956.

The author presents a typical case of Marfan's syndrome with luxation of the lenses, arachnodactily, large slender stature and a cardiac anomaly made manifest

by murmurs and electrocardiographic changes. He discusses the difficulty in optical correction when one eye is effectively aphakic and the other one normal. Unless a lens becomes totally dislocated surgical treatment is inadvisable. (3 figures, 25 references) Walter Mayer.

Stein, W. and Kikiela, M. **Two familial cases of Oguchi's disease.** *Klinika Oczna* 26:227-234, 1956.

Two cases of Oguchi's disease are described in a brother and sister. Both had night blindness from childhood. The eye grounds looked yellow and became pink only after prolonged occlusion. Occlusion of one eye alone produced a difference in the color of the eye grounds. Lack of deep reflexes in one case and increase of them in the other are evidence of a disturbance in the nervous system and a degree of skull deformity was also present. No consanguinity was found in parents. (2 figures, 15 references) Sylvan Brandon.

Stokes, J. J. **Ocular manifestations of the Sturge-Weber syndrome.** *South. M. J.* 50: 82-89, Jan., 1957.

Seven cases of hemangioma are presented: two of isolated choroidal hemangioma; one of facial hemangioma with heterochromia iridis; two of facial hemangioma with glaucoma; one of choroidal he-

mangioma with glaucoma; and one of facial angioma with retinal detachment and possibly glaucoma. Four of these seven had retinal detachments. In the last two it was possible to cause a transient rise in the intraocular pressure of the involved eye by compression of the jugular veins. (7 figures, 5 references)

Harry Horwich.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Bresslau, C. and Braga, P. **The medical record, its maintenance and its relationship to ophthalmology.** *Rev. Brasil. oftal.* 15:439-448, Dec., 1956.

This paper, written by record librarians, deals with the different systems of keeping records and makes special mention of the newer methods with perforated cards, which facilitate finding, for example, articles and book loans. (9 references)

Walter Mayer.

Orlowski, Witold J. **Polish ophthalmological literature in 1955.** *Klinika Oczna* 26:253-256, 1956.

The author lists all articles on ophthalmological subjects which appeared in the Polish medical literature in 1955; 74 titles are listed. Sylvan Brandon.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Abram Breneman Bruner, Cleveland, Ohio, died January 9, 1956, aged 65 years.

Dr. John Henry Ohly, Brooklyn, New York, died December 13, 1956, aged 79 years.

ANNOUNCEMENTS

ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1957.

The written examination will be nonassembled and will take place on Thursday, August 22nd, in certain assigned cities, and will be proctored by designated ophthalmologists.

The oral and practical examinations will be on Saturday, October 12th, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the Chairman of Examinations, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington, D.C., and must be accompanied by the examination fee of \$30.00. Applications will not be accepted after July 1, 1957.

HOME-STUDY COURSES

The 1957-1958 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, which are offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1st and continue for a period of 10 months. Detailed information and application forms can be obtained from Dr. William L. Benedict, the executive secretary-treasurer of the academy, 15 Second Street, S.W., Rochester, Minnesota. Registrations should be completed before August 15th.

ORTHOPTIC TRAINING AVAILABLE

The Ohio State University, Department of Ophthalmology, will begin the next orthoptic course in September, 1957. This is an intensive nine-month program, combining basic science and practical work. No fees are charged, but the student must support herself during the training period. Inquiries should be directed to Dr. William H. Havener, Department of Ophthalmology, Ohio State University, Columbus, Ohio.

SOUTH AND NORTH CAROLINA MEETING

The joint annual meeting of the South Carolina Society of Ophthalmology and Otolaryngology

and the North Carolina Eye, Ear, Nose, and Throat Society will be held in Hendersonville, North Carolina, on September 15, 16, 17, 18, 1957. Headquarters will be the Skyland Hotel. The following guest ophthalmologists will be on the program:

Dr. A. E. Maumenee, Baltimore, Dr. P. J. Leinfelder, Iowa City, Iowa, and Dr. Alston Callahan, Birmingham, Alabama.

The following otolaryngologists will be on the program: Dr. Francis Le Jeune, New Orleans, and Dr. J. W. McLaurin, Baton Rouge, Louisiana.

Hendersonville, North Carolina, is located in the Blue Ridge Mountains and is a particularly lovely spot at this season of the year. A large attendance is anticipated.

MISCELLANEOUS

UNIVERSITY OF KANSAS COURSE

On the guest faculty for the course in ophthalmology and otolaryngology offered by the Department of Postgraduate Medicine, University of Kansas School of Medicine, Kansas City, Kansas, were Dr. David D. Donaldson, Boston, Dr. Joseph S. Haas, Chicago, Dr. Hugh L. Ormsby, Toronto, and Dr. Lorenz E. Zimmerman, Washington, D.C.

SEMINAR ON GLAUCOMA

A seminar on glaucoma with particular emphasis on gonioscopy and the study of the anterior angle was given at the Brooklyn Eye and Ear Hospital on May 13th, 14th, and 15th. Ample opportunity for practical instruction in the use of the gonioscope was given and material from the glaucoma clinic was utilized.

The course was directed by Dr. Daniel Kravitz, assisted by Dr. Mortimer A. Lasky, Dr. Arthur Shainhouse, Dr. A. Benedict Rizzuti, and Dr. Abner S. Rosenberg.

Registration was limited to six ophthalmologists.

CONTRIBUTION FOR RESEARCH

A most significant and generous contribution for research in the diseases of the eye has been given to the University of Toronto by Herbert G. Stapells, Q.C., Toronto corporation lawyer.

His donation of \$25,000 will be used for clinical research by members of the staff of the Department of Ophthalmology in the university's teaching hospitals, and also to defray expenses of staff members for short periods of study in other research centers.

The department has received large support from government sources for its eye research program,

but few private individuals have supported clinical eye research to such an extent.

DEDICATE TEMPLE EYE CLINIC

A large group of ophthalmologists of the Philadelphia area attended a special program and open house to dedicate the new eye clinic of the Department of Ophthalmology at the Temple University Medical Center.

One of the nation's leading ophthalmologists, Dr. Algernon B. Reese, chairman of the Section on Ophthalmology of the American Medical Association, addressed the meeting on "Surgery for the relief of cataract."

Dr. Robert Robbins, professor of radiology and director of the Radiotherapy Department at Temple University Medical Center, spoke on radiation of the eye.

Under the direction of Dr. Glen G. Gibson, professor and head of the Department of Ophthalmology, the clinic includes all the modern diagnostic instruments. Special operating room equipment for eye surgery has been obtained for the operating room.

SOCIETIES

ILLINOIS MEETING

On the ophthalmic program for the 28th convention of the Central Illinois Society of Ophthalmology and Otolaryngology held recently at Champaign, Illinois, were: Dr. P. J. Leinfelder, Iowa City, Iowa, "Some typical visual field changes," "Affections of the orbital apex," and "The responsibility of the ophthalmologist in diseases of the central nervous system"; and Dr. C. L. Pannabecker, Peoria, Illinois, "Ocular pemphigus and glaucoma."

Officers of the society are Dr. Edward Albers, Champaign, president; Dr. William A. McNichols, Dixon, president-elect; Dr. William F. Hubble, Decatur, vice-president; Dr. Clarence A. Fleischli, Springfield, secretary-treasurer.

UNITED KINGDOM CONGRESS

The annual congress of the Ophthalmological Society of the United Kingdom was held at The Royal Society of Medicine, 1 Wimpole Street, London, during April. On the program were:

Presidential address: "The intraocular circulation in arteriosclerosis and high blood pressure," J. J. Healy, M.B., Ch.B.; "Symposium on congenital cataract," Mr. J. H. Daggart and Mr. A. B. Nutt, speakers; discussion on "Intravitreal vitreous in retinal detachment surgery," Mr. P. McG. Moffatt and Mr. C. Dee Shapland, speakers; "The role of the sclera in operations for detachment of the retina," Mr. George Black.

"Resection and advancement of the levator palpebrae superioris: Anterior approach: Some points in technique," Mr. H. B. Stallard; "A new instrument for taking lamellar grafts," Prof. A. Franceschetti.

Discussion on "Ocular aspects of diabetes," Prof. G. I. Scott, Dr. Norman Ashton, and Dr. J. D. N. Nabarro, openers; "Toxoplasmic uveitis," Mr. E. S.

Perkins; "A case of lacrimal obstruction," Mr. Frank W. Law; "An unusual case of Marcus Gunn syndrome," Mr. Rupert Parry.

"Ocular changes after rupture of the liver," Mr. G. T. W. Cashell; "Phacolytic glaucoma," Dr. P. B. Schofield; The Bowman Lecture: "The etiology of primary glaucoma," Sir Stewart Duke-Elder.

"Venous obstruction at the disc in chronic glaucoma," Mr. J. H. Dobree; "The foreign-body detector and locator," Mr. M. J. Roper-Hall; "A case of retinoblastoma with post-mortem findings," Mr. John Ellison; "A clinical and pictorial survey of uveitis in childhood," Mr. Joseph Minton; "The pathogenesis of onchocerciasis," Dr. F. C. Rodger; "The pattern of conjunctivitis at Moorfields during 1956," Mr. Barrie R. Jones, et al.

MILWAUKEE SPEAKER

Dr. Alston Callahan, Birmingham, was the guest speaker at the February meeting of the Milwaukee Oto-Ophthalmic Society. His subject was "Practical points in plastic surgery of the lids."

PENNSYLVANIA ACADEMY PROGRAM

The 15th annual meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology will be held May 23rd, 24th, and 25th at the Bedford Springs Hotel, Bedford, Pennsylvania. Dr. Chevalier L. Jackson, president of the academy, will preside. The guest of honor will be Dr. Edwin N. Broyles of Baltimore. Ophthalmologists participating in the program will be Dr. Philip M. Lewis, Memphis; Dr. Lorenz E. Zimmerman, Washington, D.C.; Dr. Harry S. Weaver, Jr., Philadelphia; Dr. Roscoe J. Kennedy, Cleveland; Dr. Richard E. Hoover, Baltimore; Dr. G. Victor Simpson, Washington, D.C.; and Dr. John M. McLean, New York.

MASSACHUSETTS EYE AND EAR ALUMNI

Papers of ophthalmic interest presented at the annual meeting of the Massachusetts Eye and Ear Alumni Association meeting held recently in Boston were:

"Necessity for and requirements of a surgical operating slitlamp: With presentation of a pilot model," Dr. William Stone, Jr.; "Induced sudanophilia in the guinea pig cornea," Dr. Henry Ring; "Contemporary concepts of headache, especially ocular," Dr. Hugh C. Donahue; "Incidence of Brushfield's spots," Dr. David O. Donaldson and Dr. Robert J. Herm; "Pulseless disease," Dr. Joseph L. Dowling, Jr., and Dr. Taylor R. Smith; "Uveitis in rabbits with experimental allergic encephalomyelitis," Dr. S. J. Bullington and Dr. Byron H. Waksman; "Multiple peripheral iridectomies in cataract surgery," Dr. Thomas Cavanaugh; "Calcifying epithelioma of Malherbe," Dr. Irwin S. Taylor; "How to influence people when you can't make friends," Dr. Robert D. Mattis.

"Some physical aspects of intraocular pressure," Dr. Charles J. Rife; "The action of Diamox on normal and glaucomatous eyes," Dr. Maurice Lang-

ham; "Gelfilm in glaucoma surgery," Dr. David S. Johnson; "Large polypoid growth on inner surface of each upper lid recurring whenever removed during 35 years," Dr. Frederick H. Verhoeff; "Altitudinal hemianopsia," Dr. David G. Cogan; "Eye surgery in Boston from 1820 to 1870," Dr. Virgil G. Casten; "The first alumnus, John Homer Dix," Mr. Charles Snyder; "Spontaneous intra-epithelial cysts of the iris and ciliary body and glaucoma," Dr. Paul A. Chandler and Dr. Harry E. Braconier; "Discussion on gonioscopy," Dr. Robert R. Trotter and Dr. David D. Donaldson.

Dr. Alan C. Woods, Baltimore, presented the annual Howe Lecture, his subject being "Immunologic processes in diseases of the eye."

WEST VIRGINIA ACADEMY

The 10th regular meeting of the West Virginia Academy of Ophthalmology and Otolaryngology will be held on May 21st and June 1st at the Greenbrier, White Sulphur Springs, West Virginia. On the program will be:

"Evolution of vision," Dr. Joseph Krinsky; "Eye disturbances in relation to nasal sinus diseases," Dr. Henry M. Goodyear; Round-table discussions: "When to operate in glaucoma," and "Scleral resection and buckling"; "Menière's disease as related to various types of dizziness," Dr. Goodyear.

Officers of the society are: Dr. William F. Breckner, Huntington, West Virginia, president; Dr. William F. Shirkey, Charleston, president-elect; Dr. Frederick C. Reel, Charleston, vice-president; Dr. William K. Marple, Huntington, secretary-treasurer; Dr. James K. Stewart, Wheeling, and Dr. James T. Spencer, Charleston, directors.

SOUTH CAROLINA OFFICERS

The officers of the South Carolina Society of Ophthalmology and Otolaryngology are: Dr. James H. Gressette, Orangeburg, president; Dr. Robert P. Jeanes, Easley, vice-president; Roderick Macdonald, 330 East Main Street, Rock Hill, South Carolina, secretary-treasurer.

FRENCH MEETING

The 64th session of the Société Française d'Ophthalmologie met in Paris, May 12th to 16th. The interesting contributions were not only from France but also from Algeria, America, Belgium, Bulgaria, Greece, Italy, Yugoslavia, Spain, Switzerland, and Turkey. R. I. Fried and E. Smith of Cleveland illustrated with motion pictures the Marcus Gunn phenomenon; and Ira A. Abrahamson, Jr., of Cincinnati spoke of his experience with topical metsteroids in 1,500 cases. The exhibits were impressive, as well as the operations and demonstrations shown in various hospitals.

PERSONALS

Prof. Rudolf Thiel, director of the University Clinic for Eye Diseases, Frankfurt am Main, will receive the Graefe medal at the next meeting of the German Ophthalmological Society in Heidelberg.

His Imperial Majesty the Shah of Iran has conferred upon Dr. R. Townley Paton, New York, Companionship in the Royal Order of Homayun in recognition of meritorious services to Iran. The decoration and the diploma conferring the honor were presented at the Iran Embassy in Washington, D.C.



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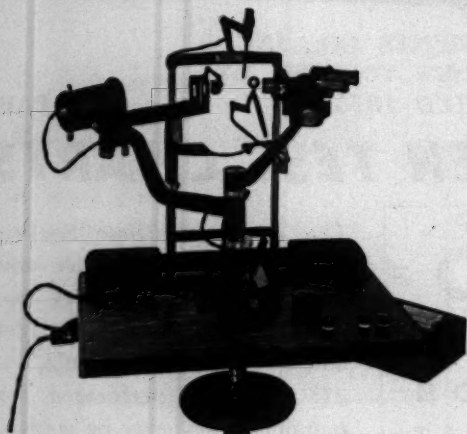
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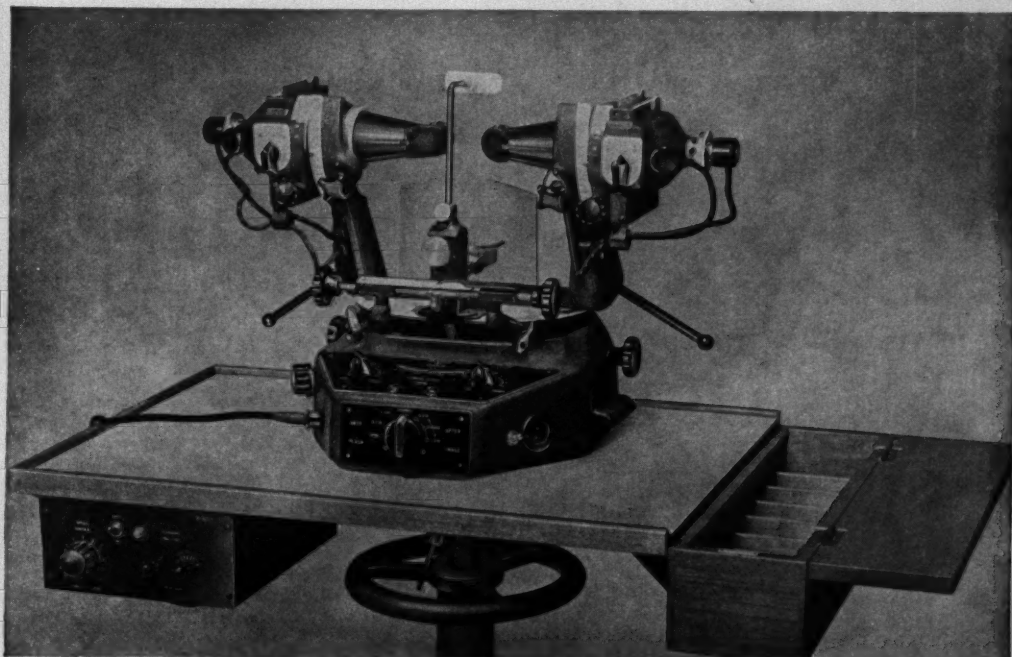
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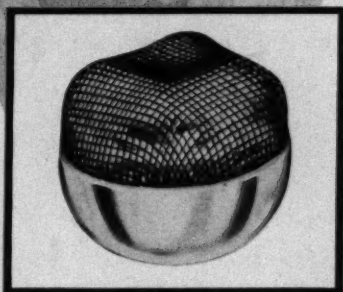
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